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RELATION OF DRUG THERAPY TO NEUTROPENIC STATES

CHAIRMAN'S ADDRESS

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In 1931 the first evidence was presented that the disease agranulocytosis was caused by the administration of certain drugs.¹ Since that time there have accumulated a large amount of confirmatory data and reports of experiments from over the world that this concept is correct. The purpose of this paper is to summarize this evidence and to make further suggestions concerning the use of some of these drugs, particularly since new preparations are being introduced constantly and at least one of them (sulfanilamide) can be definitely added to the list of offenders.

AMINOPYRINE

The incrimination of aminopyrine in the production of neutropenic diseases is based, first, on geographic studies which show that the incidence of the disease closely parallels the use of the drug; second, on the fact that the incidence is higher for the groups of the population that are the most habitual users of the drug; third, on the collection of records showing that in a large majority of patients with agranulocytosis the disease has followed the administration of the drug, and, fourth, on the administration of aminopyrine to an occasional patient who has recovered, with consequent reproduction of the disease. The fourth type of evidence adds conclusive proof that this drug is capable of producing agranulocytosis in an occasional person.

In 1935 Kracke and Parker² summarized the relationship between agranulocytosis and aminopyrine and collected 153 reported cases of agranulocytosis which had followed the use of aminopyrine. In 1937 Plum,³ in the most comprehensive review of the disease that has yet appeared, collected 267 cases in which it had apparently followed the use of aminopyrine.

The evidence incriminating this drug has been supported by clinical experiments in which patients who have recovered have been given small doses of the preparation and the disease reproduced in them. Such experiments have been carried out by Madison and

Squier,⁴ Benjamin and Biederman,⁵ Sturgis and Isaacs,⁶ Plum³ and others, and all of them demonstrated that the occasional person who has been fortunate enough to recover from the disease can have it induced a second time by the administration of even a small amount of aminopyrine. Furthermore, in nearly every case in which the disease has developed while the patient was being hospitalized for another condition, it followed the administration of this drug.

Recent clinical experiments of importance are those of Dameshek and Colmes,⁷ who studied four patients who had recovered from the disease. The first patient was given 10 grains (0.6 Gm.) of aminopyrine by mouth, had marked leukopenia and recovered. The second patient was given 10 grains of aminopyrine every two hours for five doses; there was no immediate change in the blood cells, but an attack of agranulocytosis occurred two weeks later. Another patient, after being given 10 grains of aminopyrine every three hours for three doses, presented marked leukopenia. These patients were tested by scratch, intradermal and patch tests, an aqueous solution of the drug being used, but the results were negative. However, when the same solution was mixed with blood serum and permitted to age under refrigeration, the tests with this preparation were positive. Furthermore, a second attack of the disease was produced by the intradermal injection of as little as 0.6 grain (0.04 Gm.) of this "serumized aminopyrine."

This evidence all indicates that the occasional person who acquires the disease after the administration of this drug does so on the basis of a hypersensitivity to it. Therefore it seems reasonable that the patient is allergic to the action of aminopyrine and that the amount of the drug given plays little part in the production of the disease.

This is further indicated by the report of Madison and Squier,⁴ who gave a single dose of aminopyrine to each of two patients, with marked depletion of the granulocytes, and the report of Benjamin and Biederman,⁵ who produced marked leukopenia with one dose of the drug.

An important and conclusive link in the incrimination of this drug is found in the recent report of Plum,³ in which he showed the incidence of agranulocytosis correlated with the use and sale of aminopyrine in

Read before the Section on Pathology and Physiology at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 16, 1938.

1. Kracke, R. R.: The Experimental Production of Agranulocytosis. *Am. J. Clin. Path.* 2: 11 (Jan.) 1932.

2. Kracke, R. R., and Parker, F. P.: The Relationship of Drug Therapy to Agranulocytosis, *J. A. M. A.* 105: 960 (Sept. 21) 1935.

3. Plum, P.: Clinical and Experimental Investigations in Agranulocytosis with Special Reference to the Etiology, translated by Hans Andersen, London, H. K. Lewis & Co., Ltd., 1937.

4. Madison, F. W., and Squier, T. L.: The Etiology of Primary Granulocytopenia (Agranulocytic Angina), *J. A. M. A.* 102: 755 (March 10) 1934.

5. Benjamin, J. E., and Biederman, J. B.: Agranulocytic Leukopenia: Report of a Case Successfully Treated with X-Rays; Effect of Aminopyrine, *J. A. M. A.* 103: 161 (July 21) 1934.

6. Sturgis, C. C., and Isaacs, Raphael: Observations Concerning Etiology of Agranulocytosis, *Tr. A. Am. Physicians* 49: 328, 1934.

7. Dameshek, William, and Colmes, Abraham: The Effect of Drugs in the Production of Agranulocytosis with Particular Reference to Amidopyrine Hypersensitivity, *J. Clin. Investigation* 15: 85 (Jan.) 1936.

Denmark through the years from 1925 to 1936, as summarized in the accompanying chart.

From this chart it will be seen that the consumption of aminopyrine in Denmark before the disease made its appearance was practically nil and that there was a gradual increase in the use of aminopyrine paralleling the increasing number of cases of agranulocytosis, the peak being reached in 1934. At that time the use of the drug was practically abandoned, and the disease disappeared. Plum³ concluded from his studies that aminopyrine was by far the most frequent cause of agranulocytosis in Denmark.

Many workers have endeavored to reproduce agranulocytosis in lower animals by the injection of aminopyrine and related compounds, but their experiments in general have been unsuccessful. My associates and I have injected aminopyrine in solution into rabbits, guinea pigs, dogs and rats and have fed the drug by mouth to a large number of animals but have been unable to produce a marked depression of the leukocytes in any of them.

Stenn⁸ has administered the drug by various routes to a total of 120 animals, including rabbits, guinea

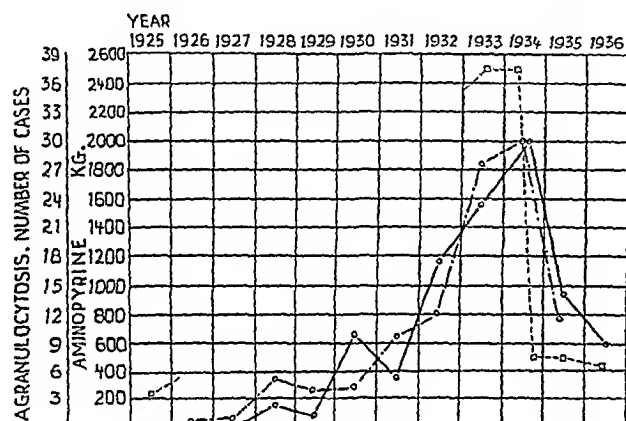


Chart showing practically complete disappearance of agranulocytosis from Denmark after the importation of aminopyrine was prohibited (from Plum³). The solid line indicates the number of cases of agranulocytosis, the dots and dashes the sale of aminopyrine from importing firms and the broken line the estimated total consumption of aminopyrine.

pigs and monkeys, but with no success in producing depression of the leukocytes. On the other hand, we have submitted the drug to an oxidation process such as conceivably might occur in the intestinal tract and have produced moderate leukopenia, but in only an occasional animal. Madison and Squier⁴ reported a marked depression of the leukocytes in only one rabbit of a total of eleven fed tablets of allylisopropylbarbituric acid and aminopyrine (allonal). Miller and Rhoads,⁹ using a total of fifteen dogs, gave some of them aminopyrine by mouth in conjunction with a blacktongue-producing diet and were able to produce acute stomatitis and anemia before these conditions would have developed from an inadequate diet alone, and they found a suppression of maturation of the bone marrow elements.

Climenko¹⁰ measured the amount of response of the leukocytes in rabbits after injection of sodium nucleinate and measured it again after the animals had been given aminopyrine and dinitrophenol. The height of

the response was much less in the drug-fed animals, and study of the bone marrow showed myeloid hyperplasia followed by suppression of maturation, with some degeneration and necrosis and finally aplasia. This would indicate that the bone marrow in its entirety has to be damaged rather severely before evidence of depression is seen in the peripheral blood and that the marrow has a large reserve power.

Many experiments have been done in an effort to show the effect of aminopyrine on groups of normal and abnormal human beings. For example, Rawls¹¹ observed the development of agranulocytosis in four of 400 patients who were receiving aminopyrine in the treatment of arthritis. Davis and Frissell¹² gave 30 grains (2 Gm.) of aminopyrine daily to thirty-two patients for from two weeks to three months with no change in the leukocyte count. In this connection Plum³ said "It has been well demonstrated that amidopyrine given to large groups of people is not followed by the development of the disease unless one of them happens to have the necessary sensitivity to the drug" and "It has been demonstrated that other drugs have no effect on the blood of persons sensitive to amidopyrine and that amidopyrine has no effect on the blood of nonsensitive persons."

There is now general agreement that aminopyrine is dangerous and that its use should be drastically restricted. Thus, Bie¹³ of Copenhagen said "If we want to avoid the risk of producing agranulocytosis, the only way is not to use amidopyrine at all," while Witts¹⁴ of England declared "Amidopyrine is a dangerous drug and all remedies which contain it should be clearly branded as dangerous drugs with the word 'amidopyrine' and not some alias" and Comroe¹⁵ of Pennsylvania suggested "that this drug be dropped from the pharmaceutical armamentarium."

DINITROPHENOL

Dinitrophenol, which has been used mainly in the treatment of obesity, can definitely be included in the list of drugs that produce neutropenic diseases. Hoffman, Butt and Hickey,¹⁶ Davidson and Shapiro,¹⁷ Dameshek and Gargill,¹⁸ Silver¹⁹ and Frank²⁰ have reported a total of seven cases, two of which were fatal. In addition, the drug is known to produce cataracts in an occasional patient, so that its use in the last two years has been curtailed to a considerable degree and reports of agranulocytosis following its use have become more infrequent.

ARSPHENAMINE

Plum has reviewed the literature of the neutropenic diseases following the administration of arspenamine with and without preparations of bismuth. In fourteen

8. Stenn, Fred: The Etiologic Relationship of Amidopyrine to Agranulocytosis, *J. Lab. & Clin. Med.* **20**: 1150 (Aug.) 1935.
9. Miller, D. K., and Rhoads, C. P.: The Effect of Diet on the Susceptibility of the Canine Hematopoietic Function to Damage by Amidopyrine, *J. Exper. Med.* **66**: 367 (Sept.) 1937.
10. Climenko, D. R.: The Modification of the Hematopoietic Function in the Rabbit by Certain Cyclic Compounds, *J. Lab. & Clin. Med.* **21**: 913 (an.) 1936.

11. Rawls, W. B.: The Effect of Amidopyrine upon the Red, White and Polymorphonuclear Blood Cells of a Series of One Hundred Patients, *Am. J. M. Sc.* **192**: 175 (Aug.) 1936.
12. Davis, J. S., and Frissell, L. F.: Amidopyrine Hypersensitivity, *J. Lab. & Clin. Med.* **23**: 107 (Nov.) 1937.
13. Bie, V.: Agranulocytosis, *Nord. med. tidskr.* **11**: 208, (Feb. 8) 1936. Quoted by Plum.
14. Witts, L. J.: Effect of Toxic Substances on the Blood-Forming Organs, *Brit. M. J.* **2**: 211 (Aug. 1) 1936.
15. Comroe, B. I.: Drugs as Etiologic Factor in Agranulocytic Angina, *Ann. Dent.* **3**: 17 (March) 1936.
16. Hoffman, A. M.; Butt, E. M., and Hickey, N. G.: Neutropenia Following Amidopyrine: Preliminary Report, *J. A. M. A.* **102**: 1213 (April 14) 1934.
17. Davidson, E. N., and Shapiro, Matthew: Neutropenia Following Dinitrophenol with Improvement After Pentnucleotide and Leukocyte Cream, *J. A. M. A.* **103**: 480 (Aug. 18) 1934.
18. Dameshek, William, and Gargill, S. L.: Studies in Agranulocytosis: Report of Two Cases of Agranulocytosis Following the Use of Dinitrophenol, *New England J. Med.* **21**: 440 (Sept. 6) 1934.
19. Silver, Solomon: A New Danger in Dinitrophenol Therapy: Agranulocytosis with Fatal Outcome, *J. A. M. A.* **103**: 1058 (Oct. 6) 1934.
20. Frank, Ira: Granulocytic Angina: Report of Three Cases with Two Fatalities, *Arch. Otolaryng.* **23**: 310 (March) 1936.

cases the hematologic defect was limited to the granulocytes and there was no anemia or sign of hemorrhagic diathesis. Furthermore, occasional reports, such as that of Blew,²¹ indicate that this drug does produce in an occasional person a hematologic and clinical syndrome that is indistinguishable from agranulocytosis. He reported this syndrome in three young white males, one of whom had received sixty-eight injections of neoarsphenamine, another a large number and a third only three.

The depressing effect of organic arsenical compounds on the bone marrow elements has long been recognized, but it should be borne in mind that these drugs are capable of producing hematologic defects limited to the granulocytes and therefore agranulocytosis.

COMPOUNDS SIMILAR TO AMINOPYRINE

As soon as the dangers of aminopyrine had become generally recognized it was to be expected that certain pharmaceutical companies would produce similar compounds in which very slight chemical changes were

made. This experiment is important because it indicates that the person who is sensitive to aminopyrine is also sensitive to novaldin, though this was to be expected because the two preparations are so nearly identical.

SULFANILAMIDE

This remarkable drug, which has proved to be of so much value in the treatment of beta streptococcus infections, is not without its dangers to the blood. These dangers include the development of methemoglobinemia and cyanosis, acute hemolytic anemia and agranulocytosis. I have found eleven cases of agranulocytosis in which the disease apparently followed the administration of sulfanilamide. These are summarized in table 1.

It will be noted that these cases have all been reported since April 1937 and that over half of the patients were young adults. In every instance a large amount of drug was administered (from 40 to 50 Gm.) before the disease made its appearance. This indicates that the mechanism of granulopoietic depression may

TABLE 1.—Agranulocytosis Following the Administration of Sulfanilamide

Date	Author	Age	Sex	Race	Amount of Drug	Leukocyte Count	Outcome	Other Drugs
April 1937	Plumer, H. E.: New England J. Med. 216:711, 1937	54	♀	W	Daily dose 33 days	W.B.C. 400 No granulocytes	Death	None
June 1937	Borst, J. G. G.: Lancet 1:1519, 1937.....	61	♀	W	45 Gm. 18 days	W.B.C. 900 Granulocytes 1%	Death	Dilute hydrochloric acid; castor oil
July 1937	Young, C. J.: Brit. Med. J. 2:105, 1937.....	53	♂	W	54 Gm. 18 days	W.B.C. 1,800 No granulocytes	Death	Salicylates
Aug. 1937	Bernstein, S. S.: J. Pediat. 11:198, 1937.....	6 mo.	♀	N	16 Gm. (orally) also injections 4 wk.	No neutrophils	Death	Not stated
Sept. 1937	McGinty, P.: Unpublished observation.....	19	♀	N	50 Gm. 18 days	W.B.C. 1,350 No granulocytes	Recovery	None
Oct. 1937	Jennings, G. H., and Southwell-Sander, G.: Lancet 2:898, 1937	39	♀	W	90 Gm. 21 days	W.B.C. 444 No neutrophils	Recovery	Not stated
Jan. 1938	O'Connell, J. T.: U. S. Nav. M. Bull. 36:61, 1938	Youth	♂	W	25 Gm. 7 days	W.B.C. 650 No granulocytes	Death	Probably more sulfanilamide
Jan. 1938	Schwartz, W. F.; Garvin, C. F., and Koletschy, S.: J. A. M. A. 110:368, 1938	32	♂	W	56 Gm. 21 days	W.B.C. 800 No neutrophils	Death	Antisiphilitic treatment
Jan. 1938	Berg, S., and Holtzman, M.: J. A. M. A. 110:370, 1938	22	♂	W	35 Gm. 16 days	W.B.C. 1,600 No neutrophils	Death	None
Aug. 1937	Mitchell, A. G., and Traehsler, W. H.: J. Pediat. 11:183, 1937	Child	Large doses	Not stated	Death	
Aug. 1937	Model, A.: Brit. M. J. 2:295, 1937.....	20	♂	W	54 Gm. 18 days	W.B.C. 600 No neutrophils	Death	

made so that the therapeutic effect would be as nearly identical with that of aminopyrine as possible and yet the preparation could be given another name. An example of such compounds is that marketed under the name of novaldin. This preparation has the same chemical formula as aminopyrine except that one of the methyl groups attached to the amino nitrogen is replaced by the sodium salt of methyl sulfonic acid.

Agranulocytosis following the administration of this preparation has been reported by Klumpp²² and by Benjamin and Biederman.²³ Ironically enough, Klumpp's patient took this preparation because his physician warned him against the dangers of aminopyrine. Benjamin and Biederman gave 10 grains of novaldin to a patient who had recovered from agranulocytosis which had followed the use of aminopyrine. Within eight hours the clinical symptoms of the disease developed, including a leukocyte count of 2,800 per cubic milli-

be different from that following the administration of a single dose of aminopyrine. In practically all these cases the leukocyte count fell to extremely low levels, with complete disappearance of the neutrophils. The usual clinical symptoms followed, and death occurred in nine of the eleven cases. In nearly all of them the administration of other leukocyte-depressing drugs could have been eliminated.

Therefore, on the basis of these reports, sulfanilamide can be added to the list of drugs that are capable of producing agranulocytosis. Furthermore, it should be borne in mind that because of the increasing use of this drug there will probably be an increasing number of cases in which the disease will follow its administration. This is especially true because the preparation can be purchased by the public in drug stores and used widely without medical supervision. Unfortunately in this connection it is similar to aminopyrine. It is reasonable to assume that the market will shortly become flooded with patented remedies containing this drug and that the dangers of agranulocytosis will become more accentuated.

I have observed two patients in whom the disease developed after the administration of sulfanilamide.

21. Blew, C. L.: A Report of Three Cases of Agranulocytosis, U. S. Nav. M. Bull. 35:484 (Sept.) 1937.

22. Klumpp, T. G.: Agranulocytosis Associated with the Administration of Novaldin, a Derivative of Aminopyrine, J. A. M. A. 108:637 (Feb. 20) 1937.

23. Benjamin, J. E., and Biederman, J. B.: Agranulocytic Leukopenia Induced by a Drug Related to Aminopyrine, J. A. M. A. 107:495 (Aug. 15) 1936.

One recovered, but the other died after the leukocyte count had fallen to 2,700 per cubic millimeter with a total absence of granulocytes.

It should be emphasized that sulfanilamide also produces a severe type of acute hemolytic anemia in many patients, the red cells occasionally being hemolyzed to the extent of from one-half to one million cells a day. Also, in some patients sulfanilamide produces a marked stimulation of the leukocytes, which may or may not

TABLE 2.—*Drugs Reported to Have Caused Agranulocytosis**

	No. of Cases
Amiopyrine.....	Over 300
Dinitrophenol.....	7
Arsphenamine.....	20
Antipyrine.....	2
Derivative of amiopyrine (oovaldin).....	2
Acetanilid ?.....	2
Acetophenetidin (phenacetin) ?.....	3
Cinchophen (atophan) ?.....	1
Antimony compound (neostibosan) ?.....	8
Sulfanilamide.....	11
Quinine ?.....	4
Gold salts ?.....	19 (Plum)

* The drugs known to be capable of producing the disease are not followed by a question mark; for the others, followed by a question mark, the evidence is not adequate.

† Hematologic depression limited to granulocytes only.

‡ Hematologic depression not limited to granulocytes.

be preceded by a moderate depression. I have observed six such patients being treated for various infectious states; the leukocyte counts reached alarmingly high figures during convalescence from the disease (74,000, 56,000, 40,000 and 25,000, with a marked granulocytic shift to the left). This indicates that sulfanilamide produces in some patients a depression and in others a stimulation of leukopoietic activity.

OTHER DRUGS SUSPECTED OF CAUSING AGRANULOCYTOSIS

In addition to the drugs discussed, which are unquestionably capable of producing the disease, certain other preparations have been suspected by various writers. These include antipyrine, which is the chemical precursor of and closely related to aminopyrine. Groen and Gelderman²⁴ have reported two cases in which agranulocytosis followed its use. Acetanilid as a causative factor has been suspected by Watkins²⁵ and Hudnutt,²⁶ and I have observed a classic attack following the prolonged administration of a patent remedy known as "Dr. Mile's Nervine," the essential ingredient of which is stated to be acetanilid. Acetophenetidin (phenacetin) has been named as the probable causative factor in two instances by Kracke and Parker² and in one by Costen.²⁷

Shapiro and Lehman²⁸ have reported agranulocytosis in one patient who was being treated with cinchophen (atophan). Quinine has been suspected as being causative in at least four instances. Zia and Forkner²⁹

treated a large number of patients for kala-azar with a proprietary preparation of pentavalent antimony compound (neostibosan), and agranulocytosis developed in eight. Plum³ has reviewed the literature concerning the danger of gold salts and collected nineteen cases in which agranulocytosis apparently followed the administration of this class of drugs. All the preparations that are known to be capable of producing agranulocytosis and those suspected of producing it in rare instances are listed in table 2.

ALLYL-ISOPROPYL-ACETYL-CARBAMIDE (SEDORMID)

Sedormid is a preparation that has become widely advocated for the relief of pain. Although it has not been reported as a cause of agranulocytosis, it has been reported as the causative factor in eleven cases of thrombocytopenic purpura³⁰ and is included here as another preparation capable of depressing the thrombocytic elements of the marrow with little effect on the leukocytes. This preparation has been termed non-acceptable for inclusion in New and Nonofficial Remedies and should be used with caution.

THE INCIDENCE OF AGRANULOCYTOSIS

In an effort to determine whether or not agranulocytosis is becoming less frequent in the United States, I have procured data from the United States Bureau of Vital Statistics relative to the deaths reported from it within the years 1934, 1935 and 1936. The figures for those years as well as for 1931, 1932 and 1933 are shown in table 3.

It will be noted that there has been very little change in the yearly number of deaths reported during the past six years. However, death reports are not a reliable index to the incidence of the disease. It can

TABLE 3.—*Deaths from Agranulocytosis in the United States*

1931.....	417
1932.....	453
1933.....	444
1934.....	503
1935.....	380
1936.....	407

TABLE 4.—*Deaths from Agranulocytosis in the Larger States*

State	1934	1935	1936
California.....	42	33	17
Illinois.....	30	17	22
Massachusetts.....	32	8	5
Michigan.....	13	9	13
Minnesota.....	13	9	8
Missouri.....	17	8	9
New Jersey.....	26	19	14
New York.....	65	51	36
Pennsylvania.....	42	25	34

reasonably be assumed that in the past three years recognition and diagnosis of the condition has become far more frequent than in preceding years. However, it could be claimed that the number of cases is larger now and that more patients recover because of better methods of treatment. It has been my experience that the condition is now rarely seen in the southeastern part of the United States.

A study of the report of the Bureau of Vital Statistics shows a decreased incidence of the disease in prac-

24. Groen, J., and Gelderman, C. J.: Agranulocytose (Maligne Neutropenie) door Drie Geneesmiddelen, Nederl. tijdschr. v. geneesk. 78: 3444 (July 29) 1934.

25. Watkins, C. H.: The Possible Role of Barbiturates and Amidopyrine in the Causation of the Leukopenic State, Proc. Staff Meet., Mayo Clin. 8: 713 (Nov. 22) 1933.

26. Hudnutt, O. D.: Case of Agranulocytosis with Recovery Following Administration of Concentrated Liver Extract, J. Michigan M. Soc. 34: 440 (July) 1935.

27. Costen, J. B.: Agranulocytosis: Appearance of the Early Pharyngeal Lesion: Three Cases, One Apparent Recovery, Ann. Otol., Rhin. & Laryng. 42: 372 (June) 1933.

28. Shapiro, Shepard, and Lehman, Lester: A Case of Agranulocytosis Following Ingestion of Cinchophen, Am. J. M. Sc. 192: 705 (Nov.) 1936.

29. Zia, L. S., and Forkner, C. E.: The Syndrome of Acute Agranulocytosis and Its Occurrence as a Complication of Kala-Azar, Am. J. M. Sc. 188: 624 (Nov.) 1934.

30. Hoffman, A. M.; Kahn, Julius, and Fitzgibbon, J. P.: Thrombocytopenic Purpura Following Allyl-isopropyl-acetyl-carbamide (Sedormid), J. A. M. A. 110: 725 (March 5) 1938.

tically all the larger states, as shown in table 4. In this connection I have solicited the opinions of several hematologists in different geographic areas of the country. There seems to be general agreement that the disease is not observed as frequently now as during recent years; this opinion is shared by Custer and Fitzhugh of Philadelphia, Heck and Watkins of Rochester, Minn., Parker of Boston, Sturgis of Ann Arbor, Mich., Haden of Cleveland and Cannon of Chicago.³¹ Madison stated that the disease has increased recently around Milwaukee, with some attacks apparently caused by sulfanilamide.

Such statistics as are available from the larger medical centers show a high peak in the incidence during the years 1933 and 1934, with a decrease up to this time, although no institution has had a sufficient number to make figures of any considerable value. Sturgis states that agranulocytosis did not commonly exist before 1922 and then had an increasing incidence, which reached its peak about three or four years ago, followed by a decline in frequency; this is affirmed by observations in large clinics in which all patients have routine blood examinations.

In view of such fragmentary evidence it seems logical to assume that agranulocytosis is decreasing in incidence, in particular that which follows the administration of aminopyrine. However, in the future this decrease may be counterbalanced by an increasing number of attacks following the administration of sulfanilamide. In view of Plum's report from Denmark, in which it is clearly shown that the incidence of the disease in that country closely paralleled the consumption of aminopyrine, there can be little doubt that the decrease in this country has been dependent on the amount of aminopyrine consumed.

Even if it is possible for all physicians to cease using aminopyrine the disease will not disappear as long as the public is able to purchase this drug over the counter in drug stores. There is much evidence to indicate that the administration of aminopyrine is being curtailed by some physicians. However, in the last case of agranulocytosis that I observed the disease followed the prolonged administration of amytal compound, yet the physician in charge assured me that he had not used aminopyrine in the treatment of this patient because he was cognizant of the dangers of that drug. Apparently he did not know that amytal compound is a mixture of aminopyrine and a barbituric acid preparation. This illustrates the deplorable tendency to prescribe drugs without knowing what they contain and indicates the extent to which pharmacology is dominated by pharmaceutical manufacturers. Aminopyrine is still included with many other preparations in compounds that have been given a variety of names, few of which indicate the presence of the drug. A list of such preparations is shown in table 5. This is an incomplete list and does not include patented remedies for the relief of pain, whose virtues are so loudly extolled over the radio and through other advertising mediums. No doubt agranulocytosis will continue to follow the administration of aminopyrine from three sources: first, from the occasional physician who prescribes it; second, from physicians who unknowingly use it when it is incorporated with other pharmaceutical agents, and, third, from the purchase of proprietary and patented remedies from drug stores by the patients themselves.

In an effort to control the incidence of agranulocytosis the physician should refrain from the use of aminopyrine or analgesic agents that contain it; second, he should warn his patients against the dangers of self medication, particularly the purchase and use of pain-relieving remedies for which the formula is not available; third, the physician who is using agents such as sulfanilamide in the treatment of severe infectious states or is using arsphenamine and other organic arsenicals should watch the patient carefully for signs of possible hematologic depression by frequent studies of the blood; fourth, the physician should take an active part in the program of public instruction relative to the dangers

TABLE 5.—Preparations That Should Be Used with Caution Because They May Depress the Leukocytes

Preparations Containing Aminopyrine	
Alonal	Dymen
Alphebin	Dyseo
Amarbital	Eu Med
Amidol	Gardan
Amido-Neonal	Gynalgos
Amidone	Hexin
Amidophen	Iprat-Amidopyrine
Amidopyrine (aminopyrine)	Kalms
Amidos	Lumodrin
Amidotol compound	Midol
Amifeine	Mylin
Aminol	Neonal compound
Am-Phen-Al	Neurodyne
Ampylin	Nod
Amytal compound	Optalidon
Analgin	Pernalga
Antabs	Phenamidal
Baramid	Phen-Amidol
Barb-Amid	Phenopyrine
Benzedol compound	Pyramidon
Cibalgin	Pyraminal
Cinchopyrine	Sequit
Combral	Yeast-Vite
Cronal	
Drugs Known to Produce Depression of the Marrow	
Dinitrophenol	Antipyrine
Arsphenamine	Sulfanilamide
Novaldin	Sedormid (thrombocytopenia)

of these preparations, for only if he does so can the public become informed as to these dangers. Certainly it will not get this information from drug stores and pharmaceutical manufacturers.

CONCLUSIONS

1. The cause of most agranulocytosis is now definitely established.
2. The disease has practically disappeared from Denmark because aminopyrine is no longer used in that country.
3. Approximately 80 per cent of drug-produced agranulocytosis is caused by the administration of aminopyrine or one of its compounds, with a lesser percentage being caused by the administration of dinitrophenol, arsphenamine, sulfanilamide, and novaldin.
4. The disease is decreasing in incidence in the United States, probably because of the more cautious use of aminopyrine by the medical profession.
5. The number of cases of agranulocytosis from the use of sulfanilamide will probably increase in the future, particularly if this drug is incorporated in patented remedies and indiscriminately sold to the public under noninforming names.
6. Physicians should attempt to prevent this disease by caution in the use of these drugs, by instruction of patients concerning their purchase in drug stores and by programs of public instruction.

31. Personal communications to the author, June 1938.

THE PRESENT STATUS OF THE SERUM THERAPY OF LOBAR PNEUMONIA

M. A. BLANKENHORN, M.D.

CINCINNATI

It is not often that the Section on Practice of Medicine requests a report on the present status of the treatment with a well known remedy of a common acute illness. Generally the best remedy soon becomes the most popular, and all physicians quickly learn which one that is. Such, however, has not been the case in the treatment of pneumonia. Apparently the recent interest in the serum treatment of lobar pneumonia has expressed itself in so many forms, other than in curing patients, that one may well ask questions about merit and popularity.

It takes a bold person to judge merit and popularity in a problem that vexes most of the medical profession in an issue that is changing with great rapidity. It is impossible to say very much in finality now. However, after a number of years of personal experience with the serum treatment of pneumonia and after a very thorough search of the current literature, I find that enough information is at hand to warrant a consideration of the present status.

A good many years of my experience have been with slow methods of pneumococcus typing and with treatment using unrefined serum of low potency. But in the past three years, i. e., from October 1935 to April 1938, my associates and I at the Cincinnati General Hospital have studied slightly more than 1,000 cases, in 230 of which potent serum was used. The fatality rate in the serum treated group was 8.2 per cent.¹ The expected fatality in this hospital and under the same circumstances of medical care as judged by 318 cases (not treated) of the same types was 34 per cent. This is a reduction of 76 per cent in fatality rate. We have treated type I and type II pneumonia mainly and these only in the early stages, i. e., before the end of the fourth day of sickness. For type I and type II pneumonia this reduction in fatality rate at the Cincinnati General Hospital just about describes the merits of serum treatment wherever it has been used consistently in early cases that are accurately typed for specificity.

Similar merit has been reported from (what should be called) the pneumonia centers in New York and Boston hospitals. In two states that have pioneered in the use of serum in the home as well as in the hospital the results are not very different. This merit of serum treatment for type I and type II pneumonia is described in all the standard textbooks of medicine of recent date and in up-to-date works on treatment. The superiority of serum treatment over all other cures should no longer be doubted.

In addition to the reports from two Eastern hospitals which have been most quoted, I find eighteen separate reports (all with adequate controls) from Ohio, Michigan, Connecticut, Pennsylvania, Canada, England, Scotland and Denmark, all attesting a 50 to 60 per cent reduction (ours is 76 per cent) in mortality rate for type I pneumonia and from 40 to 50 per cent reduction for type II pneumonia.

There is, however, considerable variation in the actual and final figures, so that if the worst results with serum in one place are compared with the best results without serum at another place, no great merit is seen in serum treatment. Such a method of estimating merit is entirely fallacious, for adequate controls are possible and have been published. I could find no report of completely unsatisfactory results from serum, save only of certain experimental serums that are not recommended for general use. It is true that serum treatment in its present form (i. e., with rapid accurate typing and potent refined serum) has been evaluated in but a few localities; but where it has been tried it is found to be good. Whether one can say good enough for all localities depends mainly on the types found in each locality. To arrive at this estimate of merit I have searched 184 current journal articles, mostly from January 1937 to the present, all recommending the use of serum.

USE OF PNEUMOCOCCUS SERUM

How popular is this treatment; i. e., how extensive has been the use of antipneumococcus serum? To judge from reports in current literature only a few individuals and a few hospitals have actually made general use of it. A questionnaire of hospitals conducted by the American Medical Association² showed that very few large municipal hospitals (where the patient ill with pneumonia is most likely to go) were typing the pneumococci in their cases of pneumonia. Questions were asked of 4,565 hospitals (2,595 hospitals replied, and only 1,850 hospitals reported being equipped to type).

A survey of my own³ on the distribution of serum for the first eleven months of 1937 shows that from an estimated number of 160,413 cases, serum was provided for 34,185 cases of type I and type II pneumonia combined. This estimate of the number of cases treated is based on the information that 3,418,500,000 units of serum was sold. Using 100,000 units as an average for one patient, we find that 34,185 patients with type I and type II pneumonia (or 21 per cent of the estimated total number of cases of these types) received serum treatment in the first eleven months of 1937. This estimate of the annual number of cases of type I and type II pneumonia, i. e. treatable types, was furnished by Dr. McGill of the United States Public Health Service in a report in 1937.

Considering the complete want of any other specific for pneumonia, there is still a considerable gap between merit and popularity (only 21 per cent treated). It is in contemplation of that gap between merit and popularity that many of the facts are to be found that are important in making progress toward pneumonia control. To me it is apparent that, wherever specific serum is being used, accurate bacteriologic diagnoses are being made and accurate vital statistics are being accumulated. By contemplating the present status of serum therapy, much may be learned about pneumonia control. If all the obstacles in the way of early diagnosis and exact bacteriologic diagnosis (typing) were understood and overcome, the progress of pneumonia control would be much more rapid.

In May 1938 THE JOURNAL published the special report of the Pneumonia Advisory Committee of the

Read before the Section on Practice of Medicine at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 15, 1938.

1. Rueggsegger, J. M.: Pneumonia: A Three Year Survey, in preparation.

2. Pneumonia Mortality and Pneumococcus Typing Facilities, editorial, J. A. M. A. 109: 1910 (Dec. 4) 1937.

3. Data on the distribution of serum for 1937 were supplied through the courtesy of Dr. W. T. Harrison of the U. S. Public Health Service, the National Drug Company, E. R. Squibb & Sons, Lederle Laboratories, Inc., Eli Lilly & Co. and Gilliland Laboratories.

U. S. Public Health Service to the Surgeon General.⁴ It was not a lengthy report, but it contained forty-nine specific recommendations in the way of studies to be made, facts to be found, experiments to be done—mainly bacteriologic—and a few social experiments as well. All these recommendations are based on the new knowledge of pneumonia that may come from the wide use of complete typing.

SUITABILITY OF SERUMS FOR GENERAL USE

Are the present serums suitable for wide and popular use? The answer is yes, if the type incidence is the same all over the country and if typing facilities are available. The actual facts in the matter of type distribution are meager, and but few cities have done the work necessary to learn what the true type incidence may be. New York, Massachusetts, Connecticut, Pennsylvania, three cities in the Middle West (Detroit, Cincinnati and Minneapolis), one on the Pacific Coast (San Francisco) and three in the South have published significant observations on type incidence. Eight large cities of the Eastern and Northern United States show from 43 to 66 per cent for the combined treatable types, I and II. But it has been generally said that upward of 50 per cent of cases are due to pneumococci of types I and II; but, so far as the literature concerned shows, 50 per cent is too high. Meanwhile other serums have been added, thus increasing greatly the so-called treatable types. Especially in the South does this rule of 50 per cent fail. Reports from four large Southern cities show that cases of type I and type II pneumonia combined range from 19 per cent to 35 per cent. Sometimes there is a considerable fluctuation as may result from a change in the plan of typing. I find that when typing is done only to search for pneumonia of types I and II, in order to ascertain whether or not serum treatment is indicated, the results may be quite different from those in laboratories charged with complete typing regardless of the hope to treat. In the one instance the laboratory is satisfied to report whether or not the physician has type I or type II pneumonia to treat, whereas with complete typing the laboratory must tell what type actually is present. This additional responsibility on the laboratory has made for thoroughness, which may greatly revise the ideas about type incidence. For instance, in one city of the South the incidence of type I and type II pneumonia combined had apparently changed from 5 per cent to 50 per cent in two years.

Another prerequisite to popular use of serum therapy is accurate typing. There has been but little use of serum reported without typing even where bivalent serum of pneumococcus type I and pneumococcus type II combined is employed. How accurate then is typing? In good hands the rapid, direct method of Neufeld seems to be very accurate. In a recent book of great merit, the late Dr. Benjamin White⁵ concluded that by this method "there should be few cultures that cannot be classified in the thirty-two fixed types." The Neufeld method applies equally to sputum, but broth cultures and mouse inoculations are frequently needed to check sputum analysis and occasionally to analyze sputum where the direct method fails. The Neufeld method, although simple and easy to learn, requires practice and patience.

4. Special Report of Pneumonia Advisory Committee to Surgeon General, U. S. Public Health Service, J. A. M. A. 110:1701 (May 14) 1938.

5. White, Benjamin: The Biology of Pneumococcus, New York, Commonwealth Fund, 1938.

Dr. James Ruegsegger, pneumonia fellow in the Cincinnati General Hospital, has trained a large group of typers for the Ohio State Department of Health as well as every one of the numerous assistant residents who came to our medical service. He finds that these students can master the technic in a week's intense work and relies on these residents for a considerable amount of emergency typing. When sputum is not obtained promptly, we use cultures made from throat swabs and find, as do others, that although slower than direct sputum typing it is a satisfactory method. Blood cultures are found very useful for routine serum therapy and in some circumstances are absolutely essential for accurate knowledge needed for treatment. Blood cultures check the accuracy of sputum typing, especially in cases in which multiple infections may occur. Blood cultures are of aid in calculating dosage, and most writers recommend that a double dose of serum be given to patients who have bacteremia.

CARRIERS

What about the carrier state and the difficult task of deciding whether a mouth organism is important or unimportant? That problem is solved by the combined experience of the bedside doctor and the typer. The gross appearance of the sputum, the scarcity of other organisms and the method of sputum collection or of throat swabbing must all be added to intelligent bedside guessing in a manner rarely practiced in any other clinical laboratory consultation. Prompt and accurate typing is absolutely essential to successful serum treatment and requires an intimate working relation between laboratory and bedside doctor that is rarely to be found, save only where some pneumonia enthusiast has worked for several years. This teamwork must be rehearsed in advance of the onset of the disease. Want of this consultation service spells failure unless the clinician does all his own typing, which is seldom possible. Laboratory delay or confusion can wreck any so-called pneumonia program.

EFFECTIVENESS OF SERUM

Is specific serum administered when accurate typing has been done generally successful? For type I pneumonia, when given early and in large doses, the answer is yes. It is so uniformly successful that if the patient does not improve one should suspect a mistake in typing or the presence of a complication, usually empyema. For type II pneumonia, even with large doses results are not so favorable, but mortality is reduced from an expected rate of 40 per cent to about 20 per cent if treatment is instituted early in the course of the disease. The effectiveness of serums for pneumonia of types V, VII and VIII seems midway between that for types I and II as reported from six separate hospitals during 1937. In our own series for 1937-1938 (which is the time we have had such serum) the result was as good as in type I pneumonia.

In all reports for all serums, the necessity of early treatment is clear. It also appears that the practice of early treatment with serum will eventually effect a definite change in the habits of doctors caring for patients with pneumonia. In diagnosis, the emphasis now will fall on history, symptoms and faint physical signs. Most of the technic of diagnosis, including x-ray as ordinarily taught and practiced, is inadequate for early diagnosis and to recognize complications.

SAFETY

Is serum safely and easily given? Since serum for adults must be given intravenously in large doses as early as possible, certain dangers must be offset by precautions. The Massachusetts Department of Public Health found four deaths among 1,313 treated patients in which the death could be ascribed to the serum. About one fourth of the patients of this series were treated in homes in Massachusetts. In our series there has been one such death among 230 treated patients. In our particular instance, obvious warnings were not seen and understood by the intern giving the serum. We practice as a routine the methods of testing for sensitivity which are accepted everywhere and recommended by Lord and Heffron⁶ as well as by Bullowa⁷ in textbooks on the serum treatment of pneumonia. We have abandoned the methods of desensitizing; but we do, in doubtful cases, give a test dose intravenously and watch the blood pressure for a drop that might presage a dangerous shock.

As to other types of serum, i. e. other numbers, especially rabbit serum, I am not so sure, but I think that in the hands of skilful physicians most patients can be treated safely with any form of serum. I have searched thoroughly most of the state journal literature up to and including May 1938 and I do not find any account of serum accidents or any warnings against the present methods now advanced, except that the State Department of Health⁸ in New York did issue a warning in *THE JOURNAL* about the general use of rabbit serum.

I find a trend to shorten the intervals between doses and to raise the dose, especially for type II pneumonia. We now treat many of our patients with but two doses, one of 20,000 units and an hour later one of 60,000 or 80,000 units of type I. For type II pneumonia we generally give 20,000 then 60,000, 60,000 and 60,000 at hourly intervals.

In all cases in which blood cultures are positive we administer, as does every one, twice the usual dosage. This supplementary dose is usually given on the following day, as blood cultures require from twelve to twenty-four hours for incubation. We do not assign to an expert the giving of serum. All our interns and residents give it as a part of the hospital routine. Sensitive or doubtfully sensitive patients are treated by interns but under immediate supervision of the fellow in pneumonia. In passing I may describe our hospital as a city hospital without a special pneumonia service and without many of the facilities that university hospitals enjoy. The cost of the serum is borne by public funds, but the laboratory is maintained and the director provided by private funds.

COMPLICATIONS

What about serum therapy and complications? Early successful serum treatment prevents and cures pneumococcic septicemia and in this manner reduces the incidence of suppurating complications. If such suppuration has already started before serum treatment has been completed, horse serum is probably of no value. This want of value in pneumococcic suppuration may not be true of rabbit serum. Even with large doses, a considerable percentage of serum failures is found to

be due to undiscovered empyema. All writers with experience emphasize the importance of searching out early empyema. We have learned that serum is of no value in endocarditis, and we were unsuccessful in treating pneumococcic meningitis.

SUMMARY

Complete typing of all cases, through the entire thirty-two types, is the keystone of serum treatment and may provide the necessary information leading to the prevention of pneumonia.

In parts of the United States where typing has been practiced, treatable types comprise more than 50 per cent of all cases of pneumonia, save only in certain districts of the South. Now that other therapeutic serums (V, VII, VIII and probably many more by the device of rabbit serum) have been developed, a much higher percentage will be treatable.

Neufeld typing of the sputum and cultures of various body fluids is a rapid and accurate method of bacteriologic diagnosis of pneumococcus types.

The selection of patients for efficient and satisfactory treatment requires early diagnosis by the physician and intimate consultation with the bacteriologist. Serum must be given in adequate dosage by vein, and a double dose must be given when blood cultures are positive. Serum must be injected slowly after sensitivity tests are found negative, but the entire dose should be given during the first twenty-four hours. Serum accidents have been extremely uncommon and the danger of reactions early and delayed should rarely preclude treatment.

Refined and concentrated horse serum for type I and type II pneumonia is a well established and satisfactory remedy. When given during the first twenty-four hours it is a specific comparable to the best specific biologic remedy, save only diphtheria antitoxin. When given within the first four days of the disease, the mortality rate of pneumonia may generally be reduced more than 50 per cent. In our experience of three years the mortality was reduced 76 per cent.

Until 1937 the use of serum treatment, as judged from published results, was restricted to a few places—Massachusetts, New York, Maine, Connecticut, Ohio and Michigan. In 1937 approximately 20 per cent of patients with type I and type II pneumonia in the United States were treated with serum.

Cincinnati General Hospital.

ABSTRACT OF DISCUSSION

DR. EDWARD S. ROGERS, Albany, N. Y.: In regard to the arbitrary selection of a period of four days from the onset of the disease as being the crucial interval for serum treatment, our experience in New York State has added a little further information. In the specific treatment of 2,027 type I cases, we have found that we can extend that period of usefulness to include the fifth day, the case fatality rate for cases treated on that day being, roughly, 16 per cent. One must be cautious in attempting to predict the incidence of pneumonia and particularly of individual types in the anticipated experience of any particular community. I am not sure how Dr. McGill, whom Dr. Blankenhorn quotes, derived his figures, but the basis on which such calculations usually are made is rather questionable. Dr. Blankenhorn has suggested such caution and also the futility of assuming that the type incidence once established for any given area will necessarily remain the same for that area. Dr. McLaughlin of Pittsburgh has told me that in his experience in the past three years he has encountered a change in the incidence of type II pneumococcus pneumonia from about 5 per cent to

6. Lord, F. T., and Heffron, Roderick: *Pneumonia and Serum Therapy*, Revised Edition, New York, Commonwealth Fund, 1938.

7. Bullowa, J. G. M.: *The Management of the Pneumonias*, New York, Oxford University Press, 1937.

8. Warning Against Premature Use of Rabbit Serum for Pneumonia, *J. A. M. A.* 110: 747 (March 5) 1938.

about 35 per cent. In New York State we have observed massive shifts in the prevalence of type specific pneumonia in a number of areas during the past few years. The use of repeated sputum specimens is unquestionably worth emphasis. A patient treated early and adequately with specific serum who does not respond to that treatment within a period of from twelve to eighteen hours may well be subjected to a complete bacteriologic reexamination. Under such circumstances another type of pneumococcus often may be found. In this respect the proper use of blood cultures will also prove of great value. Time does not permit a discussion of the problem of sensitivity to horse serum, though I imagine it might interest this group particularly. I would like to say, however, that we are finding the significance of the skin test and the ophthalmic test rather difficult to understand in relation to reactions subsequently encountered. In our type I experience, however, fatalities in any way related to serum administration, whether anaphylactic or more vague in nature, were encountered in less than 0.5 per cent of all cases. There were no deaths from chill or thermal reactions in the entire series.

DR. FRANCIS G. BLAKE, New Haven, Conn.: One of the most frequent questions encountered is What shall be the size of the initial dose? I noticed that Dr. Angevine included 50,000 units within the range of a large dose. I would consider 50,000 units a quite small initial dose, as we rarely use less than 100,000 units. The second important question is How late in the disease is it worth while beginning the use of anti-pneumococcus serum? I should like to ask Dr. Blankenhorn his opinion on that. The third important question that often arises is How long shall serum therapy be continued in a patient who has not shown clinical response after 200,000 or 300,000 units? It would be interesting to know Dr. Blankenhorn's opinion from his own experience.

DR. JAMES L. DUBROW, Des Moines, Iowa: It is important to know, when dealing with a case of pneumonia, how the diagnosis is made. Emphasis was laid on the bacteriologic examination of the sputum. However, some patients may be carriers, or the sputum may be scanty. In my opinion a chest roentgenogram shows important early signs in suspected cases of pneumonia. In some cases of early pneumonia physical examination may disclose a rale or two and one may think the chest is normal, yet the stereogram shows a patch of haziness which is a possible sign of beginning pneumonia. For corroboration in doubtful cases the chest roentgenogram should be repeated some hours or a day later, when an opacity may be shown occupying one or two lobes. Furthermore, the history of the case should be taken into consideration. Highly significant is the onset of the illness. Some claim that in lobar pneumonia atelectasis is demonstrated on the roentgenogram. The question of atelectasis is closely bound up with that of bronchostenosis. If the patient has not had a sudden acute illness, one may be dealing with a bronchogenic tumor. It may not be a case of pneumonia at all. Early blood cultures should be made, especially when the sputum is scanty or the sputum typing gives contradictory results. In such cases it is well to do a lung puncture, remove a little serum and have it examined bacteriologically for pneumococci. Once one has decided that one has a case of pneumococcal pneumonia and knows the type causing it, the question of serum therapy arises. It is well to take into consideration the leukocyte response, temperature rise and how ill the patient looks. Before administering serum it is important to determine by history, skin and conjunctival tests whether the patient is allergic. I have had cases of type I pneumonia in which the patients (some allergic) got along nicely without serum.

DR. M. A. BLANKENHORN, Cincinnati: I am indebted to Dr. Rogers for pointing out that the fourth day is not critical and that one should include the fifth day. Selection of patients was determined by economic reasons rather than epidemiologic ones. It was not possible to afford the serum for everybody, so the early cases, in which the most good could be done, were treated and the fourth day was arbitrarily chosen. Dr. Rogers emphasized the importance of typing. There seems to be a hope in wishful thinking that we won't need to type because eventually a single serum or chemical will do for all types. Certainly the trend now is for type specific serum and the

"typing" of patients for treatment absolutely essential. Dr. Blake asked a pertinent question with regard to the size of the initial dose. This dose is 20,000 units. I regard that as a testing dose. Then in one hour after the first dose I give the second dose, which may be 60,000 units or even 80,000 units, so the entire 100,000 is given within two hours. I expect to get the entire dosage in the vein within a few hours, unless the blood culture is found to be positive, in which case the repeated dose, which is equal to the first dose, is given within twenty-four hours. "How late to start treatment?" I have no opinion on that. Late treatment was not given because we couldn't afford it and because the importance of coming into the hospital early has been emphasized. "How long to continue treatment after 200,000 or 300,000 units has been given?" I have not set a time. I rarely give serum after the second day, unless blood cultures are positive. I generally stop on 300,000 units, and I have had so few failures that the question of going on with more serum rarely arises. When it does, complications are looked for. Early cases, of course, are being treated. Dr. Dubrow answered his own question when he asked about the diagnosis and then immediately mentioned the history. I think that for early recognition of the disease the history is more important than physical signs. The roentgenogram is of importance only in confirmation. The patients in our medical service are examined repeatedly and we think the most important physical sign for early diagnosis is the crepitant rale. The history and sputum are of a great deal more importance.

APNEA OF THE NEWBORN AND ASSOCIATED CEREBRAL INJURY

A CLINICAL AND STATISTICAL STUDY

FREDERIC SCHREIBER, M.D.

DETROIT

It is with some temerity that a neurologic surgeon undertakes to address an obstetric section on the subject of cerebral injury in the newborn. The two specialties have a common responsibility, however, to the child showing clinical evidence of such injury, and if either can contribute anything to reduce the number of these tragedies a critical analysis of the subject is certainly desirable.

The evidence obtained during this study indicates that cerebral asphyxia at birth may cause permanent degenerative changes in the brain with clinical neurologic manifestations. The correlation between recent neuropathologic, pharmacologic, physiologic and obstetric observations may be traced. From experience and research it is found that most cases of cerebral birth injury are associated with apnea at birth.

The significance of the association may be clarified by means of a schematic diagram showing the relationship between the stages of oxygen deficiency and results of that deficiency and the possible degrees of cerebral damage from a deficient oxygen supply. The causes and effects of various degrees of fetal anoxemia are represented in figure 1. The circle represents a wheel the segments of which turn only to the left. The hub of the wheel is the respiratory center in the

The Research Laboratory of the Children's Fund of Michigan assisted in the production of this paper.

Owing to lack of space, this article has been abbreviated for publication in THE JOURNAL. The complete article will appear in the author's reprints.

Read before the Section on Obstetrics and Gynecology at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 15, 1938.

Constructive criticism and encouragement were given by many of my colleagues, in particular Drs. George Kamperman, Nathaniel Gates, Joseph B. De Lee, Norman Miller, Ward Seely, Lewis Daniels, Owen Foster, Nathan B. Eddy, Louise Eisenhardt, Gabriel Steiner, Frank Murphy, David Levy, Edgar Mahter, W. C. Cole, W. L. Brosius and the research departments of Parke Davis & Co. and Eli Lilly & Co.

medulla. This center, first described by Legallois in 1812, depends for its proper function on the interchange of oxygen and carbon dioxide. The factors that are known to depress the respiratory center are oxygen want, drugs, gases and organic change. The obstetric counterparts of these depressing agents are normal birth trauma, abnormal birth conditions, operative intervention, oxytocics, analgesic drugs and anesthetic gases. The arrows pointing to the respiratory center indicate the degree of depressing effect on the center by these agents in relation to the clinical effect on the newborn.

The quadrants designated as phases I, II, III and IV relate the changing situations in the fetal cerebral oxidation processes. Phases III and IV, especially, concern the neurologist, since these phases include the clinical manifestations of disturbed cerebral function. The line between phases III and IV has been designated as the vital line. This line indicates the division between

if anoxemia is shown to be dangerous in itself. The most vital and rapid effect of anoxemia is on the brain, where isolated groups of cells may quickly die if there is an oxygen want (anoxia) in the tissues. Such localized cell death is irreparable and can be seen microscopically if the baby perishes. However, these localized areas of necrosis resulting from cerebral anoxia do not necessarily cause the death of the fetus or infant. In case of survival the clinical evidences of localized necrotic lesions or their resultant intracerebral scars and atrophy are neurologic disturbances whose pattern depends on the location and extent of the damaged areas.

Since the analgesic drugs employed during labor are a frequent cause of dangerous apnea in the newborn, it seems that, if brain damage is later found in cases in which considerable analgesia has been used, this injury can properly be ascribed, either wholly or in part, to the optional drugs that have been given to the mother in labor.

During a ten year period (Jan. 1, 1928-Dec. 31, 1937) 685 patients were seen in whom a relationship was suspected between the manner of birth and the later neurologic manifestations of damage to the brain. Most of these patients were seen at the Children's Hospital of Michigan, Detroit, and the remainder were seen in consultation. Of the 685 children, 131 were seen because of convulsions, sixty-nine because of spasticity, 130 for mental retardation, 248 because of combinations of these symptoms and the remaining 107 for miscellaneous neurologic conditions.

Cases subject to suspicion of postnatal infection or trauma were excluded from the group, as were those in which congenital or familial factors might have significance in cerebral symptomatology: associated meningocele, harelip, familial feeble-mindedness, erythroblastosis, hemorrhagic disease and congenital heart disease. Finally, the group was limited to those infants born in one

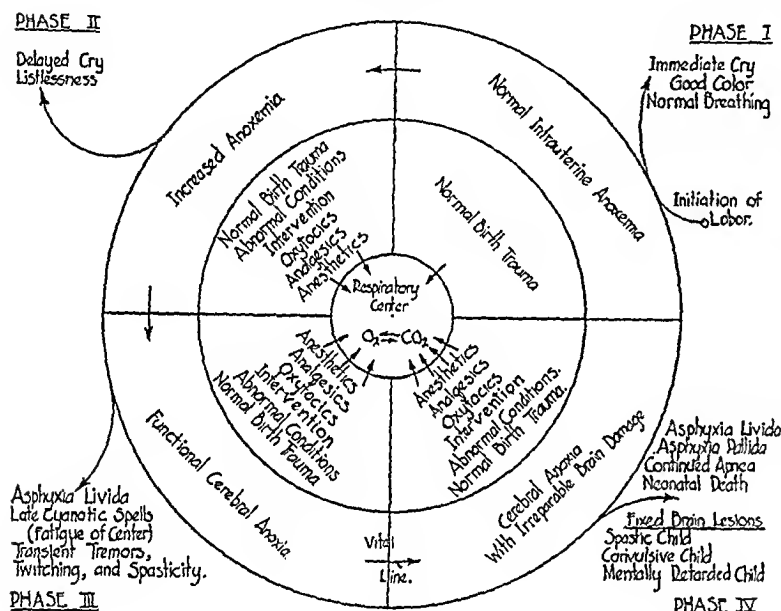


Fig. 1.—Schematic representation of the correlation between the incidence and extent of apnea and the occurrence of cerebral symptoms.

transient neurologic manifestations and irreparable damage to the brain in the newborn.

The "wheel" is set in motion by the initiation of labor. The extent of its rotation before birth varies in every case, depending on the occurrence of such unpredictable factors as the incidence of natural birth difficulties; the weight, second stage metabolism, and blood oxygen capacity of the mother, and, in addition, her individual susceptibility to the drugs and anesthetics employed to abolish pain.¹ The temperature existing in the mother and in her environment during labor and delivery must be considered. A further flip of the wheel by a depressing dose of an analgesic drug may spell the difference between a normal and a permanently damaged baby if the vital line is crossed. It appears to me that the effect of chance, in some of the cases studied in which anesthetics and analgesic drugs have been employed in labor, has been allowed to participate to such an extent as to be somewhat disturbing to the professional conscience.

Since apnea is a clinical indication of anoxemia, it must be regarded as dangerous to the newborn infant

county during the ten year period. These restrictions left 500 cases in the study group.

Study of the records for the group immediately showed that 155 of the babies were born under conditions over which a physician has little or no control: precipitate, breech, twin or premature deliveries. For some cases all the birth data were obtainable—the obstetric difficulties and the oxytocics, analgesia and anesthesia used. In others, although it is known that the mothers were given "shots" and "pills" the amounts are not known. When not available from the birth records, information on the condition of the infant at birth was given by a parent when the child was brought in because of neurologic manifestations. Only histories of apnea were accepted in which the baby was reported as remaining "black" or "blue" for a considerable period after delivery, there were recurring "blue spells," or the infant did not breathe and had to be resuscitated.

The occurrence of apnea in the group of 155 infants born under uncontrollable circumstances (precipitate, breech, twin and premature delivery) is recorded in table 1 in relation to the type of delivery used.

In table 2 the occurrence of apnea is related to the various adjuvants used during the process of childbirth.

1. Schreiber, Frederic, and Gates, Nathaniel: Cerebral Injury in the Newborn Due to Anoxia at Birth, *J. Michigan State M. Soc.* 37: 145 (Feb.) 1938.

The remaining 345 subjects of the 500 were all full term infants; in this group there were no precipitate, breech or twin deliveries. Table 3 presents the relationship between the type of delivery and the occurrence of apnea for all the 345 whose condition at birth was known. Of the 345 infants in this group, 180 were known to have been born in the hospital and 135

posed of precipitate, breech, twin and premature deliveries is greater than in the full term group.

From table 5 it can be seen that the majority of cases in this group (500) showing evidence of cerebral damage presented one factor in common—apnea at birth. The term apnea is used in its broadest sense and includes all cases in which there was delayed

TABLE 1.—Type of Delivery Related to Apnea in Those of the 345 Cases of Full Term Pregnancies for Which the Data Were Available in Which the Child Later Showed Cerebral Symptoms

Type of Delivery	Condition at Birth			Apnea at Birth	Late Apnea: Condition at Birth		Birth and Late Apnea	Total Apnea
	Known	Good	Unknown		Known	Unknown		
Spontaneous.....	140	68	27	53	8	1	19	51
Forceps.....	105	33	18	56	10	2	16	84
Cesarean.....	2	..	1	2	2
Version-extraction.....	18	2	2	10	6	16
Unknown.....	13	1	27	7	..	3	5	15

TABLE 2.—Relationship Between the Occurrence of Apnea in the Group of 155 Cases of Precipitate, Breech, Twin and Premature Deliveries in Which, After Delivery, Symptoms of Cerebral Damage Were Seen: Analgesia and/or Anesthesia—and Induction—Used During Childbirth

	Condition at Birth			Apnea at Birth	Late Apnea: Condition at Birth		Birth and Late Apnea	Total Apnea	Incidence of Apnea, per Cent
	Known	Good	Unknown		Known	Unknown			
No anesthesia or analgesics.....	23	10	2	8	2	..	5	15	65.2
Analgesics only.....	2	2	1	..	1	1	50.0
Anesthesia only.....	15	12	..	5	3	..	1	9	50.0
Anesthesia and analgesics.....	29	9	2	13	2	1	7	23	6.7
Anesthesia known, analgesics unknown...	9	3	..	5	1	6	
Anesthesia unknown, analgesics unknown	25	4	31	17	..	5	4	26	
Anesthesia known, shots and pills.....	9	2	..	4	3	7	
Anesthesia unknown, shots and pills.....	4	1	..	2	1	3	
.. .. .	10	3	1	3	2	1	4	10	90.9
	7	5	..	1	1	..	1	3	42.9
	10	6	1	3	2	..	1	6	60.0

TABLE 3.—Type of Delivery Related to Apnea in the Group of 155 Cases in Which the Data Were Available

Type of Delivery	Condition at Birth			Apnea at Birth	Late Apnea: Condition at Birth		Birth and Late Apnea	Total Apnea
	Known	Good	Unknown		Known	Unknown		
Spontaneous.....	180	34	22	37	6	3	9	55
Forceps.....	11	3	7	5	1	1	3	10
Cesarean.....	2	2	2
Version-extraction.....	20	5	7	8	1	..	7	16
Unknown.....	6	..	7	3	..	2	3	8

TABLE 4.—Relationship Between the Occurrence of Apnea in 345 Full Term Infants Who, After Delivery, Showed Symptoms of Cerebral Damage; Analgesia and/or Anesthesia—and Induction—Used During Childbirth

	Condition at Birth			Apnea at Birth	Late Apnea: Condition at Birth		Birth and Late Apnea	Total Apnea	Incidence of Apnea, per Cent
	Known	Good	Unknown		Known	Unknown			
No anesthesia or analgesics.....	7	5	..	2	2	28.6
Anesthesia only.....	57	31	..	18	3	..	8	30	51.7
Anesthesia.....	86	40	2	33	10	1	13	57	65.5
Anesthesia.....	1	1	1	
Anesthesia.....	23	7	4	11	1	..	5	17	
Anesthesia unknown, analgesics unknown	56	10	60	36	2	4	10	52	
Anesthesia known, shots and pills known.	34	10	..	16	2	..	8	26	
Anesthesia unknown, shots and pills known.....	10	2	..	6	2	8	
Medical induction.....	28	13	2	10	3	..	5	18	64.3
Surgical induction.....	7	2	..	2	1	..	3	6	85.7
Oxytocies.....	46	22	4	16	6	2	8	32	66.7

were known to have been born at home; for thirty the birthplace was not recorded.

The incidence of apnea within this group in relation to various forms of adjuvant treatment during childbirth is tabulated (table 4).

In table 5 the data from tables 2 and 4 on the occurrence of apnea are summarized and given in the percentage of those cases about which information was available. The incidence of apnea in the group com-

respiration, asphyxia livida or asphyxia pallida was evident or resuscitation was required. Of the 500 cases analyzed in the tables it may be seen that apnea in some degree was present in approximately 70 per cent of the cases in which the condition at birth was known. Fourteen mothers are known to have received nitrous oxide, 211 received ether and forty-eight received nitrous oxide-ether anesthesia. In the forty-five cases of these two groups (total group of 500) in which

no analgesia or anesthesia was used, 38 per cent showed evidence of apnea at birth or within the first few days. It must be remembered that all these patients are abnormal, with cerebral symptoms. The incidence of apnea in all the full term babies, born spontaneously, without drugs or anesthesia, during 1936 at Herman Kiefer Hospital, Detroit, was 5.76 per cent, approximately one seventh of the occurrence in the neurologically abnormal group.

Apnea indicates the presence of some degree of anoxemia with its attendant cerebral anoxia, but serious

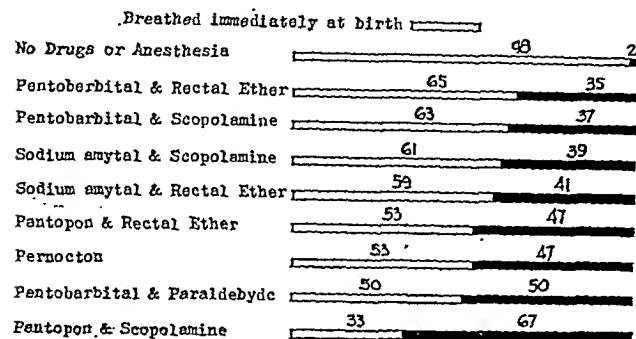


Fig. 2.—Barbiturates and hypnotics in labor; effect on initial respirations of infants.

anoxemia may be present without clinical evidence of apnea. It would seem that apnea is undesirable from the clinical standpoint since it appears in such a high percentage of cases that later show evidence of damage to the brain. Apnea is commonly found in a higher percentage of cases when analgesia and anesthesia are employed in labor than when no analgesia or anesthesia is used.² This fact is graphically illustrated in figure 2, adapted from the work of Irving, Berman and Nelson.³ These authors state that, "all methods [of analgesia] used delayed the initial respiration of the infants to some extent, since a control series of cases in which delivery was effected without any anesthetic showed only 1.9 per cent of infants who did not breathe immediately at birth."⁴

Regardless of the associated conditions in the cases of suspected cerebral birth injury under consideration, the majority were recruited from those infants who did not breathe immediately at birth—a group comparable to those represented by the blacked-in areas in figure 2.

One of the toxic effects of all drugs used to produce analgesia in labor is depression of the respiratory center.⁵ Snyder and Rosenfeld, working with animals, have shown the depressing effect of analgesic drugs administered to the mother on intra-uterine respiratory movements. Such cessation of respiratory movements may be taken as an index of anoxemia, since, according to Haldane and Priestley,⁶ "no existing physical or

chemical method of discriminating differences in reaction approaches in delicacy the physiological response to the breathing." It may be assumed that intra-uterine asphyxia may take place under similar circumstances in the human fetus. A large initial dose of an analgesic drug may depress the respiratory center of the mother to such a degree that a dangerous anoxemia ensues in the fetus, with resultant anoxic changes in the brain. However, the interval between the administration of the drug and the birth of the fetus may be of sufficient duration to allow the respiratory center of the fetus to reestablish itself, even though cerebral damage has already resulted, and the anoxemia that existed in utero is therefore not evident when the infant is born.⁷ Although permanent degenerative cerebral change may have taken place in such cases, the respiratory center itself was probably spared and normal breathing was observed at birth. Anoxemia, however, makes the respiratory center susceptible to fatigue,⁸ and this may be the explanation for the frequent occurrence of late apnea in these cases.

I have applied the term "asphyxia occulta" to the particular group of cases which came with evidence of damage to the brain and in which, during labor, a dose of analgesic drug had been given beyond the ordinary pharmacologic dosage, although the infant's record of birth showed no signs of apnea. This group of patients includes many of the apparent inconsistencies in the correlations between the administration of analgesics and anesthetics and the occurrence of apnea. Apnea of the mother necessarily results in anoxemia of the fetus. Anesthetists generally agree that the cyanosis shown by mothers under the influence of analgesic drugs improves when they come to the birthroom and receive oxygen with anesthesia. Fetal brain tissue, being more sensitive to narcotization, probably is the first to suffer anoxic changes if the drug-induced respi-

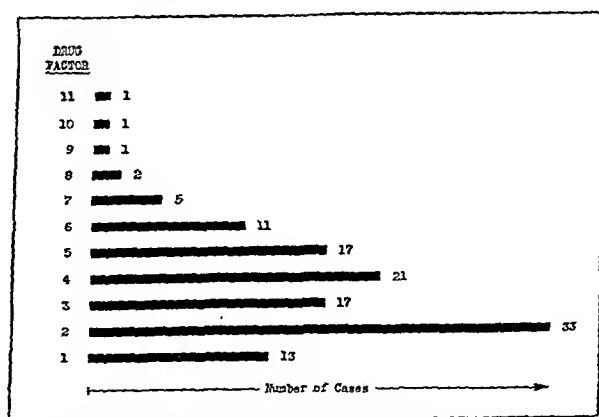


Fig. 3.—Maximum drug factor of analgesics administered in any eight hour period during childbirth to mothers of 122 babies who later showed evidence of cerebral damage.

ratory depression is severe enough.⁸ Some mothers have shown permanent cerebral change following analgesic delivery when the child also showed evidence of cerebral damage. In other cases the child apparently showed no evidence of cerebral damage, although the mother showed neurologic symptoms following analgesic delivery.¹

2. Eastman, N. J.: *Fetal Blood Studies: V. The Role of Anesthesia in the Production of Asphyxia Neonatorum*, Am. J. Obst. & Gynec. 31: 563 (April) 1936.

3. Irving, F. C.; Berman, Saul, and Nelson, H. B.: *Barbiturates and Other Hypnotics in Labor*, Surg., Gynec. & Obst. 58: 1 (Jan.) 1934.

4. In a series of 1,523 births, which included all the infants born alive in one hospital during the year 1936, a total of 139 infants, born spontaneously without any analgesia or anesthesia, are comparable to the series of Irving and his associates.² Eight, or 5.8 per cent, of the infants in this group were cyanotic.

5. Rosenfeld, Morris, and Snyder, Franklin: *Effect of Anesthetics on Fetal Respiration*, J. Pharmacol. & Exper. Therap. 57: 139 (June) 1936.

6. Eastman, N. J.: *Panel Discussion on Cyanosis in the Newborn*, J. Pediat. 9: 262 (Aug.) 1936. Snyder, Franklin, and Rosenfeld, Morris: *Direct Observation of Intra-Uterine Respiratory Movements of the Fetus and the Role of Carbon Dioxide and Oxygen in Their Regulation*, Am. J. Physiol. 119: 153 (May) 1937.

7. Haldane, J. S., and Priestley, J. G.: *Respiration*. New Haven, Conn., Yale University Press, 1935, p. 97.

8. Clifford, S. H., and Irving, F. C.: *Analgesia, Anesthesia and the Newborn Infant*, Surg., Gynec. & Obst. 65: 23 (July) 1937.

8. Jung, P. (of Göttingen): *Der Uebergang von Arzneimitteln von der Mutter auf den Fetus*, Therap. Monatsh. 28: 104 (Feb.) 1914.

No attempt has been made to determine the exact role of dystocia, operative intervention, intracranial hemorrhage and the use of oxytocics, anesthetics or analgesics and whether these are responsible for cerebral damage at birth.⁹ I wish merely to emphasize the fact that apnea, from whatever cause, may be dangerous to the fetal brain. Cerebral anoxia has been found to cause intracranial hemorrhage even though trauma is not a factor.¹⁰ Drugs that inhibit labor are also a causative factor in the present increased need for intervention.¹¹ Thus, analgesics and anesthetics, which are optional therapeutic auxiliaries, are probably the cause, in some cases, of intracranial hemorrhage—and certainly of increased surgical intervention.

Various drugs and combinations of drugs were used to obtain birth analgesia in this series of cases. In 122 deliveries for which the exact drugs, doses and times of administration are known, the distribution was as follows: morphine alone seven, morphine and barbiturates seven, morphine, scopolamine and barbiturates eleven, barbiturates alone nineteen, scopolamine and barbiturates nineteen, scopolamine alone twenty-eight and morphine and scopolamine thirty-one.

TABLE 5.—Incidence of Apnea in the Two Groups of Cases in Which Data Concerning Apnea Were Available, Tabulated in Percentage, and the Composite of the Two Groups

	345 Full Term Deliveries	155 Precliptate, Breech, Twin, and Premature Deliveries	500 Composite Group
Apnea at birth.....	61.7	63.9	62.3
Late apnea.....	8.6	11.2	9.4
Apnea at birth and later.	16.8	18.5	17.3
Total apnea.....	68.9	72.0	69.9

When barbiturates were used in combination with scopolamine, the dosage that was usually followed was the one that has been described by Irving, Berman and Nelson:⁸

The initial dose of sodium amytal by mouth was from 9 to 12 grains, depending upon the weight of the patient. This drug was repeated three to four hours later in from 3 to 6 grain doses if indicated. Forty-five minutes after the initial dose of sodium amytal one one-hundredth or one one-hundred and fiftieth of scopolamine was given subcutaneously and was repeated later as soon as the patient began to complain of pain.

The initial dose [pentobarbital and scopolamine] is from $4\frac{1}{2}$ to 6 grains by mouth which may be increased, if desired, and it is repeated according to the same indications as govern the use of sodium amytal.

If scopolamine alone was used, the dosage advocated by Daniels and Tamblyn,¹² based on their experience in 453 cases, was usually followed:

One 1/100 of a grain (of scopolamine) is given every half hour for 3 doses and then one 1/100 grain every two hours. . . . The average dose of scopolamine was 5 1/100 grain. The smallest dosage given which resulted in complete amnesia was 2 1/100 grain and the largest dose used in this series was 21 1/100 grain.

Such obstetric dosages¹³ are difficult to reconcile with the ordinary clinical doses as defined by the pharmacologist.¹⁴ The ordinary hypnotic dose of sodium amytal is from 3 to 9 grains (0.2 to 0.6 Gm.) at intervals of not less than six hours. The hypnotic dose of pentobarbital is given as from $1\frac{1}{2}$ to 3 grains (0.1 to 0.2 Gm.), with severe intoxication from doses over $7\frac{1}{2}$ grains (0.5 Gm.).¹⁵ Severe toxic effects with respiratory depression from 3 grains of pentobarbital have been reported.¹⁶

Of scopolamine, Sollmann¹⁶ states in his 1937 manual: "There are great individual variations in the response to scopolamine and therefore in its toxicity. The variable toxicity is due mainly to idiosyncrasy, for it occurs in the purest samples." He further says: "Small doses (1/300 to 1/75 grain) have produced serious poisoning with cardiac and respiratory collapse.



Fig. 4.—Generalized cerebral atrophy in an idiot with asphyxia pallida at birth.

. . . With ordinary individuals it is not safe to exceed 1/120 grain, repeating this smaller dose every six to eight hours if necessary."

The ordinary clinical adult pharmacologic dose of the drugs known to have been employed in this series of cases in which cerebral damage was encountered has been assigned a factor value of 1 for purposes of comparison with other cases in which combinations of drugs were used. If the dose used was greater than the ordinary clinical dose, the factor was increased by the proper multiple (or fraction).

9. Data on this subject were accumulated during the study but must await further analysis before publication.

10. Yant, W. P.; Chornyak, John; Schrenk, H. H.; Pátty, F. A., and Sayers, R. R.: Pub. Health Bull. 211, Studies in Asphyxia, U. S. Treasury Department, August 1934.

11. Young, James: Maternal Mortality and Maternal Mortality Rates, Am. J. Obst. & Gynec. 31:198 (Feb.) 1936.

12. Daniels, L. E., and Tamblyn, E. J.: Scopolamine Alone for the Relief of Pain During Labor, J. Michigan State M. Soc. 32:553 (Oct.) 1933.

13. Literature published by the firms manufacturing drugs usually advocates much smaller doses than are used by many practitioners. However, these firms do not hesitate to quote the dosages published in obstetric papers.

14. Cushney, A. R.: A Textbook of Pharmacology and Therapeutics, ed. 11, Philadelphia, Lea & Febiger, 1936. Gutman, Jacob: Modern Drug Encyclopedia and Therapeutic Guide, New York, Paul B. Hoeber, Inc., 1934. Sollmann.¹⁵

15. Sollmann, Torald: A Manual of Pharmacology, ed. 5, Philadelphia, W. B. Saunders Company, 1937, pp. 373-374, 737.

16. Willcox, William: The Uses and Dangers of Hypnotic Drugs Other Than Alkaloids, Brit. M. J. 1:415 (March 10) 1934.

If combinations of drugs were used, the combined factors were added. For example, morphine one-fourth grain (0.015 Gm.) (factor 2) and scopolamine $\frac{1}{120}$ grain (0.0005 Gm.) (factor 1) would give a combined drug factor of 3 in this case.

The usual doses of various drugs used have been assigned the factor values given in table 6.

Because of the difficulty in properly evaluating the effect of time, since in most cases the warnings of the pharmacologist regarding the repetition of doses within certain time limits were ignored, I was able to compare the cases only on the basis of the maximum amount of analgesics given in any eight hour period. The drug factors for the 122 patients during the eight hours of maximum administration are shown in figure 3.

It must be borne in mind that this discussion on the effects of drug dosage refers to adults who happen to be in labor. The fact that they are in labor does not protect them against the effects of toxic doses. The usual and most alarming effect is respiratory

expected to respond if orthopedic procedures were attempted. If the cerebral loss was found to be too extensive, the mentally retarded child was regarded as needing institutionalization.

Figure 4 is a reproduction of an encephalogram showing generalized atrophy of cerebral tissue in an idiot born with asphyxia pallida.

MICROSCOPIC CEREBRAL CHANGES IN STILLBORN AND NEONATAL ASPHYXIAL DEATHS

Yant and his co-workers¹⁰ fully described the microscopic changes of anoxic cerebral lesions in animals. These typical microscopic changes of the brain, which Courville¹⁷ later demonstrated in the human being as associated with cerebral anoxia, were found in infants in whom asphyxia has been present for some hours or days. Eisenhardt¹ has pointed out such changes in the brain of a stillborn infant, and more recently Steiner¹⁸ has demonstrated similar "devastation areas" in the brains of newborn infants who perished with evidence of asphyxia (figs. 6 and 7).

Figure 7 shows a section taken from the medulla of an infant who died with convulsions on the third day after birth. There had been numerous apneic spells with cyanosis dating from birth. Dr. Steiner describes the histologic changes:

In the medulla oblongata, involving the dorsal and lateral margin, a circumscribed area is present, the shape of which

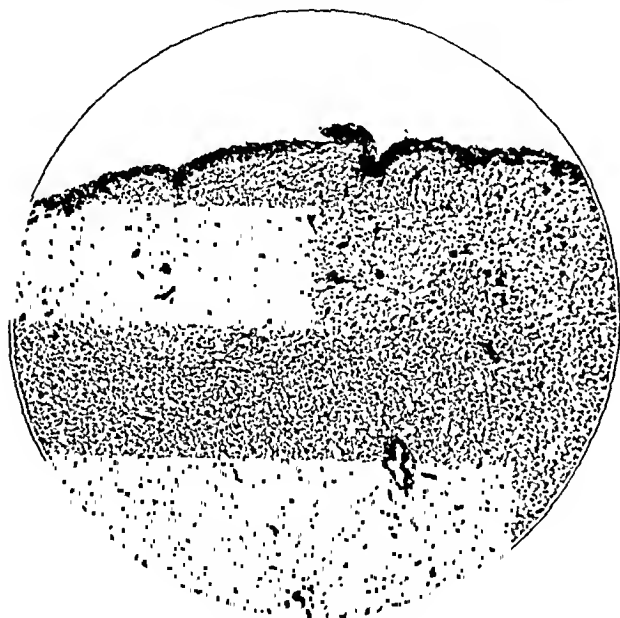


Fig. 7.—Necrosis in section of medulla of an infant cyanotic from birth.

depression. If the mother must contend with drug-induced respiratory depression in addition to the natural exigencies of childbirth, the fetus must also, being dependent on the mother for its oxygen supply until actually born, suffer from the same respiratory depression and at the same time go through the intensely traumatic experience of being born.

GROSS CEREBRAL CHANGES ASSOCIATED WITH ASPHYXIA AT BIRTH

The late microscopic changes of cerebral anoxia are death of neural tissues with gliosis.¹⁰ The gross end result is atrophy of the brain. Such atrophy can often be demonstrated by means of the encephalogram. Pneumographic studies were made on 207 of the infants in this series, of which seventy-three showed generalized atrophy, seventy-five showed localized atrophy, thirty-five showed no demonstrable changes in the roentgenograms and twenty-four of the studies were technically of no diagnostic value. These studies were usually made to determine whether the degree of cerebral atrophy was such that a spastic child could not be

TABLE 6.—Factor Values for Usual Doses of Various Drugs

	Dose, Grain	Factor
Morphine sulfate.....	$\frac{1}{8}$	1
Morphine sulfate.....	$\frac{1}{4}$	2
Scopolamine.....	$\frac{1}{120}$	1
Pentobarbital sodium (nembutal).....	$1\frac{1}{2}$	1
Pentobarbital sodium (nembutal).....	6	4
Sodium amytal.....	3	1
Sodium amytal.....	9	3

is oval and the color paler than the surrounding tissue. The size of this area is 0.6 mm. in length and 0.16 mm. in width. The limits of the lesion are sharply defined and quite regular. This area is characterized by a looser meshwork of the glial ground substance, the spaces between the meshes being empty.

A few ganglion cells are seen which show a very definite process of degeneration as evidenced by homogenization and vacuolation of the cytoplasm, pyknosis and decentralization of the nucleus, which is here located in the peripheral part of the ganglion cell. A nerve cell shadow indicating total degeneration of the cell is also present in this area.

The histologic picture is typical for the first stage of a devastation area. The location of this lesion in the medulla oblongata near the nuclei of the tenth nerve may be of particular significance.

SUMMARY

In a series of 500 patients, seen because of cerebral symptoms, approximately 70 per cent of those whose birth record was available had a history of apnea. There was a history of precipitate, breech, twin or premature delivery for 155 of the 500 infants; 345 were full term infants. In those of the group of 155 about whom data were obtainable, approximately 64 per cent had apnea at birth, 11 per cent had late apnea only and 18 per cent had both early and late apnea. The total incidence of apnea in this group was 72 per cent.

In the group of 345 full term infants, the incidence of apnea in the cases presenting a known history was

17. Courville, C. B.: Asphyxia as a Consequence of Nitrous Oxide Anesthesia, *Medicine* 15:129 (May) 1936.
18. Gabriel Steiner, research professor of neuropathology, Wayne University College of Medicine, Detroit.

at birth, 62 per cent; late, 9 per cent; early and late, 17 per cent, and total, 69 per cent.

The depressing effect, on the respiratory center, of birth analgesics given in greater than pharmacologic doses bears a direct relationship to the degree of apnea. The extent of the apnea has a direct relationship with the severity of the cerebral symptoms after birth. The severity of the cerebral symptoms is in direct relation to the amount of damage to the brain tissue. From these relationships it appears that analgesics given in greater amounts than the pharmacologic dosage may in many instances be the causative factor of fetal anoxemia, with resultant cerebral damage in the infant.

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ABSTRACT OF DISCUSSION

DR. C. B. COURVILLE, Los Angeles: My interest in asphyxia has been largely in its pathologic manifestations. This study by Dr. Schreiber would seem to strengthen the conception that the lesions of asphyxia are essentially the same regardless of the mechanism or cause of depression of the respiratory and cardiac centers. Subtotal destruction of the occipital (calcarine) cortex as a result of asphyxia can be demonstrated. This cortical area seems to be particularly sensitive to the reduction in oxygen supply. Laminar degeneration is a slightly less advanced type of lesion. Several laminae of necrosis in the cortex tend to fuse, particularly in the superficial part of the convolution. These foci of necrosis tend to occur about dilated blood vessels, which are obviously larger than those in the apparently normal regional tissues. The presence of these distended vessels in the areas of necrosis suggests that stagnation is one of the factors in producing the ultimate effects of asphyxia. It should be said that asphyxia in the newborn is due to excessive depression of the respiratory and at times the cardiac centers, that necrosis of the cerebral gray matter will occur if spontaneous breathing is absent for any length of time, that this necrosis is not demonstrable histologically unless the infant survives for at least thirty-six to forty-eight hours and that this necrosis is probably responsible for many of the residual symptoms in children that survive. As Dr. Schreiber has emphasized, the respiratory center may be dangerously depressed by anesthetic agents and drugs used in relief of pain during delivery as well as by mechanical means. Excessive depression with such agents is probably less likely to occur in well organized clinics than in deliveries in smaller hospitals or in the home.

DR. J. C. LITZENBERG, Minneapolis: Dr. Schreiber has shown that we are too apt to evaluate our results by immediate considerations only, ignoring more remote consequences. Ever since I observed the extremely high percentage of asphyxiated babies in the Freiburg clinic, where Koenig and Gauss developed "twilight sleep," I have been apprehensive of such extreme cases of apnea. Dr. Schreiber has proved that my apprehensions were justified because the remote consequences are found by the brain surgeon to be serious brain injury. When we do an operation in gynecology, we do not estimate our results by the patient getting off the table alive; we estimate our results by the remote consequences. Have we cured the patient of that for which we operated? In this late furor of painless childbirth, I have no intention of criticizing the relief of pain in labor; but this paper emphasizes that we must evaluate the individual to whom it is safe to give it, the individual to whom it is unsafe to give it, and the remote dangers of apnea following the use of any analgesic. I was impressed when I read the text of this full paper that the majority of all the author's cases in which considerable damage was done had one factor in common; that is, apnea at birth, 72 per cent of them. The 68 per cent who had no analgesia but had apnea also showed the same brain damage. Apnea is evidently a dangerous condition, perhaps more dangerous remotely than immediately. The table which showed the deliveries accomplished without any anesthetic or any analgesia showed only 2 per cent of apnea while with all the different analgesic drugs the cases of apnea ranged from 35 to 67 per cent. Therefore, on the average, when analgesics

are used, apnea occurs from seventeen to thirty-three times as often. If the author's thesis is correct, which I believe it is, it behooves us to reevaluate our attitude toward analgesics in labor with the remote as well as immediate results in mind. I feel convinced that he has established his thesis that the degeneration of the cerebral tissue is positively demonstrated and that analgesia beyond the same pharmacologic dose is a causative factor in the fetal anoxemia with the resultant cerebral damage. There are many lessons that can be learned from this paper. The one that has impressed me most is that the question of relieving the pain of labor must be reevaluated, the remote results and not only the apparent immediate results being kept in mind.

DR. CHARLES E. GALLOWAY, Evanston, Ill.: For about five years I have tried my best to look at this problem in a rational manner, because I feel that women in childbirth deserve to have as much of the pain relieved as possible with safety. But I think that physicians must be very careful in the use of analgesics in childbirth, because it is an added factor in fetal mortality. However, whenever one looks at any problem one must look at it as a whole and not from any one standpoint, and I think the pain of childbirth can be safely relieved, at least the intense suffering can be taken from the patient, without damage to the infant. When I heard about this paper I wrote a letter to every man who has taken care of any babies out of Evanston Hospital over the last five years and also to our leading neurologist in the community, who takes care of practically every case of infant mental deficiency. The letter in part was as follows: "In Detroit, and I presume other places in the country, men have been using large doses of scopolamine repeated as many as six times during labor, together with as much as 6 grains of pentobarbital. Consequently, they have had a high fetal mortality. But ever more important, they have found a small percentage of these babies mentally defective or at least constituting what might be called problem children. Those doses of $\frac{1}{100}$ grain of scopolamine repeated time after time is, I think, an abnormal medical procedure, and we at the Evanston Hospital have seldom ever given more than $\frac{1}{250}$ grain of scopolamine at any time, and it has been practically never repeated. We seldom give more than 6 grains of pentobarbital, and only occasionally does it run up to 9 or 10½ grains. Since the five and one-half years we have been using these drugs, they have been administered to only 60 per cent of the patients delivered, and there have been only two maternal deaths among the patients receiving the drugs. Please tell me what you think about the possibility of any mental damage in these babies. I expect to sum up the various answers and incorporate them in my discussion." I received about eleven answers out of thirteen letters, and the consensus among the men who have been treating such cases is that mental damage does not occur. Why the authors get so many cases in one community I cannot see, but I should like to make two statements. One is that such a procedure during labor, of giving repeated large doses of scopolamine, is very poor medical practice. The other is that I think these men have not entirely proved their thesis. I think that more work will have to be done and one will have to compare the incidence of mental damage in cyanotic babies with the incidence of mental damage without cyanosis at birth. Since the world began, about 2 per cent of the population has been born defective mentally and it may even be that a baby is cyanotic at birth because it is mentally deficient. I also believe that one expects a baby with cerebral hemorrhage to be unable to breathe.

Hippocrates' Clinical Records.—The writings of Hippocrates were copied and recopied for centuries, used by Galen, and, more or less garbled, studied almost up to the eighteenth century, when critics began to use them chiefly for historical material. Clinical records of forty-two cases have come down to us from Hippocrates, so clearly treated that Osler and Sydenham took them as model records. Among these cases were quinsy, diphtheria, typhoid fever, pleurisy, dislocations of bones, and injury to the skull.—Hurd-Mead, Kate Campbell: *A History of Women in Medicine*, Haddam, Conn., the Haddam Press, 1938.

PROCTOLOGIC TUMORS

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AND

C. A. HELLWIG, M.D.

WICHITA, KAN.

Most modern hospitals have accepted the principle of examining microscopically all tissue removed by operation. While gynecologists adhere to this rule regardless of the size of the specimen, most proctologists regard histologic study as unnecessary when small amounts of tissue are removed, especially when hemorrhoidectomy is performed.

During the last six years we have studied by microscopic methods every specimen removed during ano-rectal operation, no matter how small the lesion and how harmless its gross appearance. Reviewing our clinical and pathologic records of 951 proctologic patients, it is evident that in the majority of cases nothing has been detected by histologic study which changed the prognosis or treatment based on clinical examination. This, however, is true also in the fields of major surgery and gynecology. There are, on the

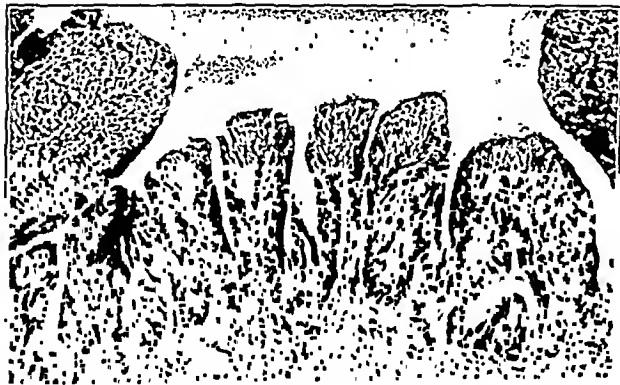


Fig. 1.—The intermediate zone of the anal canal is lined with epithelium resembling bladder epithelium. It is a remnant of the fetal cloaca. There were four papillary tumors in this area among our cases.

other hand, so many cases in our material in which the microscopic examination revealed conditions which were not suspected clinically that the routine histologic study of proctologic specimens seems well justified, in the interest of the patient.

McCarty,¹ basing his statistics on 150,000 surgical cases, found that routine microscopic examination revealed in 0.5 per cent of all operations a malignant condition which was not suspected by clinical methods or during operation. In our series of 951 proctologic cases this percentage of clinically unrecognized cancer is almost four times higher, namely 1.9 per cent. The conclusion therefore is justified that, more than in other regions, early malignant lesions of the anal canal may closely resemble harmless conditions.

There is considerable confusion in the literature regarding the anatomic limitations of the anal canal. We follow the definition of Rosser,² who regards as anal canal the lower portion of the rectum. It coincides with the pars perinealis of the anatomic nomen-

clature and extends from the perineal flexure of the rectum to the anus. It is narrowed by the sphincters and levators and is the site of anal disease. While the anal canal forms a physiologic and pathologic entity, histologically it is a complex structure. Its interior surface is lined with three different forms of epithelium which are of different fetal origin. The upper zone of the anal canal has typical intestinal epithelium with columnar cells and Lieberkühn glands. The middle or intermediate zone is a remnant of the fetal cloaca and is lined with transitional epithelium as found in the urinary bladder and urethra. This zone extends from the recto-anal line down to the anocutaneous or dentate line. The crypts of Morgagni and the anal ducts are the most important structures of this area. The distal portion of the anal canal is purely ectodermal and is called the cutaneous zone.³

Buie⁴ limits the term anal canal to only this portion which is lined with squamous epithelium. No glands are found in this zone. Sweat glands of large size, the so-called apocrine glands, sebaceous glands and hair follicles characterize the beginning of true skin or perianal region. The junction between the cutaneous zone of the anal canal and of the perianal region is called anus according to the anatomic nomenclature of Basel. To understand the great variety of anal tumors one has to keep in mind the three different types of epithelium lining the anal canal and its complex fetal development.

The uppermost zone of the anal canal is the favored site of glandular neoplasms. In our series there were fifteen adenomas and thirty-five adenocarcinomas. In the intermediate zone, which is more predisposed to inflammatory lesions than other parts of the anal canal, tumors are relatively rare. We found four benign papillary tumors resembling bladder papilloma, one melanoma and two adenocarcinomas in this area. Distal from the anocutaneous zone there were, in our series, four squamous cell carcinomas, one melanoma and one basal cell carcinoma.

Connective tissue tumors did not show predilection for different portions of the anal canal as did the epithelial growths. There were twelve benign and six malignant tumors. Besides lipomas, fibromas and myomas we found one hemangio-endothelioma, one myxoma, one xanthoma and one myosarcoma, one spindle cell sarcoma and two lymphosarcomas.

Many of the malignant tumors in our material were small and eighteen of the fifty-two malignant tumors were discovered during routine histologic examination of what seemed clinically harmless anal lesions. Two adenocarcinomas and the basal cell carcinoma were completely removed by hemorrhoidectomy and in the specimen removed at the subsequent radical operation after the histologic diagnosis was established no trace of malignant tissue could be detected.

In six of our fifty-two malignant cases, cancer developed in previously existing anal lesions. One adenocarcinoma was found originating in a fistulous tract, one squamous cell carcinoma in a fissure, three adenocarcinomas in hemorrhoid nodules and one basal cell carcinoma in an external hemorrhoid.

In 1931 Rosser² reported thirteen cases of anal malignant growths which had some benign pathologic condition as the etiologic agent and further reviewed an

From the Department of Proctology and Pathology, St. Francis Hospital.

Read before the Section on Gastro-Enterology and Proctology at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 13, 1938.

1. McCarty, W. C.: The Study of Fresh Tissue as an Aid to Clinical Diagnosis, *S. Clin. North America* 5:701 (June) 1925.

2. Rosser, Curtice: The Etiology of Anal Cancer, *Am. J. Surg.* 11: 328 (Feb.) 1931.

3. Tucker, C. C., and Hellwig, C. A.: Histopathology of Anal Crypts, *Surg., Gynec. & Obst.* 58:145 (Feb.) 1934. Tucker, C. C., and Hellwig, C. A.: Anal Ducts, *Arch. Surg.* 61:521 (Oct.) 1935.

4. Buie, L. A.: Practical Proctology, Philadelphia, W. B. Saunders Company, 1937.

additional eighteen cases from the literature which showed some anorectal disease as a forerunner. Of Rosser's thirteen cases, the etiologic factors in seven were fistula, in four hemorrhoids and in two cryptitis and papillitis. Buie and Brust⁵ in 1933 reported fifty-one cases of anal malignancy in which thirty-four showed some benign anal lesion as a forerunner. In 1937 T. E. Smith⁶ published the results of a review of the literature and personal correspondence with leading proctologists. In his report there are 107 cases of anal



Fig. 2.—The dark tumor at the right appeared clinically as a thrombosed hemorrhoid nodule. Microscopically it was a malignant melanoma.

malignancy developing from benign lesions. He does not include adenomatous polyps, which are generally recognized as precancerous conditions.

Our material of adenomatous polyps could be classified with one exception by histologic criteria as either benign or frankly malignant tumors. Only one polyp showed atypical glands in a small area, probably a transitional stage of a benign into a malignant growth. The fact that hypertrophic anal papillae are often confused with adenomatous polyps has been stressed in a recent paper by Tucker⁷ of San Antonio. In several cases the diagnosis of adenoma was made by an occasional proctoscopist, when the location in the dentate line and the whitish surface characterized these structures as enlarged papillae. We agree with Tucker⁷ that hypertrophic papillae do not carry a serious prognosis as compared with adenomas.

Not infrequently, patients seek proctologic advice while their symptoms are caused by extra-anal conditions. The complex embryologic changes occurring in the sacral region explain the origin of chordoma (two cases in our material), teratoma (one case) and dermoid cysts. Of pelvic tumors which produced symptoms calling for proctologic examination were one ovarian dermoid which became infected and perforated into the rectum, and one adenomyoma of the rectovaginal septum. A patient with a tumor of the cauda equina consulted first the proctologist on account of anal discomfort. Of interesting tumors in the perianal region we observed a sweat gland adenoma, a myxoma and a hemangioneuromyoma of the glomus type.

REPORT OF CASES

CASE 1.—History.—Mrs. H. J., a widow aged 64, admitted to St. Francis Hospital Jan. 15, 1931, had complained of hemorrhoids for the past thirty years. There was no history of bleeding but the patient complained of constipation and constant

5. Buie, L. A., and Brust, J. C. M.: Malignant Anal Lesions of Epithelial Origin, *Journal-Lancet* 53: 565 (Nov. 1) 1933.

6. Smith, T. E.: The Relation of Anorectal Diseases to Malignancy, *Proc. Dallas County M. Soc.*, Sept. 9, 1937.

7. Tucker, V. C.: Comparison of Hypertrophied Anal Papillae and Rectal Polyps, *Texas State J. Med.* 32: 810 (April) 1937.

pain in the back. On examination internal and external hemorrhoids were found. Operation was performed January 16 and tissue was sent to the laboratory.

Pathologic Examination.—There were five nodules of different size, the largest one 1 cm. in diameter, the smallest 4 mm. The surface of the nodules was folded and apparently not ulcerated. No suspicious changes were evident to the unaided eye.

Microscopic examination disclosed that the epithelium of four nodules was of typical appearance, representing either columnar or transitional epithelium. There were slight inflammatory changes in the subepithelial tissue, and large blood-filled spaces were found in the stroma. In one nodule which was taken from the junction between squamous and columnar epithelium there were glands of irregular structure. The lining cells were not well oriented and the nuclei were hyperchromatic. In a few glands several layers of epithelial cells were found. No basement membrane could be made out. These atypical cells had invaded the submucosa and had reached in one place even the muscular layer. Few of the alveoli were filled with mucoid material and exfoliated epithelial cells. No mitotic figures were found. The areas of atypical proliferation were surrounded by round cells.

The pathologic histologic diagnosis was adenocarcinoma at the junction of the squamous and columnar epithelium in one of five hemorrhoid nodules.

The patient was given high voltage roentgen therapy and radium. The radiologist reported that from January 26 to January 31 he administered 600 roentgens, using 15 and 20 cm. portals, a filter of 0.5 mm. of copper and 1 mm. of aluminum, 65 cm. tube distance, from 180 to 200 kilovolts, 8 milliamperes and twenty-five minute treatments. February 2 he administered 50 mg. of radium in a T applicator in the rectum for forty-eight hours. Feb. 18, April 8, Nov. 25, Nov. 28, Dec. 1, Dec. 8 and Dec. 19, 1931, and March 12, 1932, ultraviolet treatment was given. There has been no recurrence to date.

CASE 2.—History.—G. W., a white man aged 67, entered the proctologic department of the clinic Sept. 13, 1935, and on rectal examination a fistula in ano was found together with internal and external hemorrhoids and infected anal ducts. The patient complained of pruritus ani.

X-ray examination was negative. The patient stated that he had a chill about once a week. He had a severe chill about three months before, associated with gallbladder colic. X-ray



Fig. 3.—Hemangioma of anal canal. Clinical diagnosis, hemorrhoid.

examination showed nonvisualization of the gallbladder and no evidence of stone. The patient had chills and fever as a child when he came to Kansas. A malarial smear gave negative results. On the following day operation was performed at the County Hospital.

Pathologic Examination.—The solid nodule was composed of very atypical glands, which were invading the muscle layer. The epithelium lining the glands showed malignant characteristics. The cells were in several layers and poorly oriented. The nuclei were large and vesicular and had large nucleoli. The stroma was extremely scanty and showed round cell infiltration. In one section a hypertrophied papilla was found

with marked round cell infiltration of the subepithelial tissue. At the proximal base of the papilla, inflammatory changes were found near a duct.

The pathologic diagnosis was adenocarcinoma.

Six weeks later a perineal excision was performed. No evidence of cancer was obtained on microscopic examination. The patient has remained well to date.

CASE 3.—History.—R. C., a white man aged 43, a sales manager, first noticed bleeding from the rectum two years before. The bleeding was small in amount and occurred at irregular intervals. The bowel movements were regular. Pain began about the week previous to admittance to the hospital. Physical examination gave negative results. Proctoscopic examination revealed infected anal ducts, an enlarged papilla at the anorectal line anteriorly which resembled a tumor, and internal and external hemorrhoids. The patient was admitted to St. Francis Hospital Nov. 29, 1937, and operated on the following morning.

Pathologic Examination.—There were eleven specimens varying in size from 2 cm. to 5 mm. Three were covered with skin. Several had large blood vessels.

Microscopic examination revealed several large papillae with markedly hypertrophic epithelium and round cell infiltration. The epithelium showed parakeratosis. There were several ducts with definite inflammatory changes in the wall. The

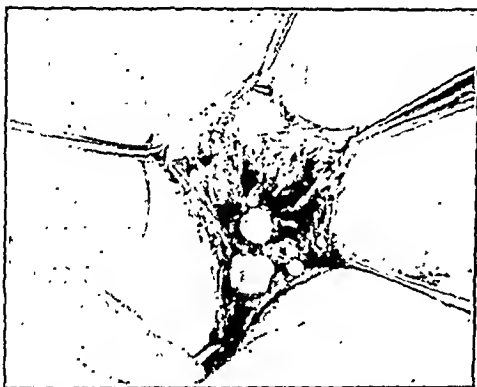


Fig. 4.—Two fibromas and one lipoma in anal canal.

internal and external nodules had large blood vessels with thin walls. No inflammatory changes were found in the skin. In one hair follicle extensive proliferation was noticed. The cells were invading the surrounding tissue and there was formation of small cysts. The structure was that of early basal cell carcinoma.

The pathologic diagnosis was external and internal hemorrhoids and infected anal ducts, hypertrophic papillae and minute basal cell carcinoma.

The patient was given high voltage roentgen therapy and radium. Jan. 5 to Jan. 12, 1938, 3,414 roentgens was administered; 15 by 15 and 20 by 20 cm. portals were used with 1 mm. copper and 1 mm. aluminum filter, 50 and 60 cm. tube distance, 185 kilovolts and 8 milliamperes. January 22, 50 mg. of radium was administered in the rectum in a rectal applicator in two layers of rubber rotated 120 degrees every four hours for twelve hours, 12 by 50, or 600 milligram hours.

The patient will continue to be examined proctoscopically every two months. There has been no recurrence to date.

CASE 4.—History.—Mrs. L. J., aged 45, white, American, a housewife, for the past two years had had some pain in the rectum but no bleeding. Four years before she had a hysterectomy for uterine fibroids, which on microscopic examination showed no evidence of malignancy. She was admitted to the hospital in May 1937 for a rectal operation. A diagnosis was made of internal and external hemorrhoids, with a papilloma at the anorectal line. There were several internal hemorrhoids and thrombosis of external hemorrhoids.

Pathologic Examination.—The section showed well preserved surface epithelium consisting of squamous cells with some hornification of the superficial layer. In the subepithelial stroma cross sections of two anal ducts were found. They were lined

with transitional epithelium. The lower third of the section consisted of an atypical glandular growth. The tumor consisted of ducts which varied in size and form. There were many solid strands without lumens. The tumor cells were poorly differentiated. They were cuboid and varied in size and staining quality. Some mitotic figures were found. There was no evidence of secretory activity. The stroma between the ducts was extremely scanty. There were no inflammatory changes. The location of the glandular growth and the presence of two typical anal ducts suggested the origin of this adenocarcinoma in the anal ducts.

The pathologic diagnosis was adenocarcinoma of the anal canal originating in anal ducts.

SUMMARY

The clinical and histologic study of 951 proctologic cases emphasizes the wide range of pathologic possibilities causing anal symptoms and the close resemblance between harmless and the most malignant anal lesions. One third of our malignant lesions were discovered by routine histologic examination of clinically benign lesions. Rosser's² theory that cancer may develop in long standing benign anal lesions was substantiated by six of our own cases.

A comparison of the clinical and pathologic diagnoses in our 951 cases proves the value of routine microscopic examination in proctologic practice.

ABSTRACT OF DISCUSSION

DR. CURTICE ROSSER, Dallas, Texas: Those who have attended the meetings of this section during the past five years will recognize that this is the third of a series of clinico-pathologic papers presented by these authors, a valuable type of report in which the clinical observations of one author are synchronized with the gross and microscopic study of his confrère. In my work in the wards of Baylor University Hospital in Dallas for some years I have noticed this association of benign lesions in the anal canal. In a recent analysis of twenty-five cases of cancer of the anal canal I found that in 87 per cent of them there was an associated benign lesion. There are certain ex cathedra statements which get into the literature more or less casually, which are repeated and copied from one paper or textbook to another, until it would seem that it would require a charge of dynamite to extricate them. Such a statement was that of Paul Kraske, some fifty years ago, that he saw no particular evidence that benign lesions of the anal canal were etiologic agents in cancer. That statement, unsupported by any evidence, has been copied in at least a hundred papers. It crept into the first edition of a standard textbook on tumors, for example, and it has gone through four editions without any change in that textbook. This fact is the reason for presenting evidence that a benign growth in the anal canal may precede and in some way cause the following malignant lesion. As Drs. Tucker and Hellwig have shown, routine biopsy is absolutely essential in the surgery of all presumably benign lesions. Practically one third of their cases of malignancy were discovered in apparently benign lesions, and that, I believe, is sufficient warrant for our insistence on this particular premise.

DR. L. E. BROWN, Corona, Calif.: That all apparently benign lesions of the rectum and anus should be sectioned and studied under the microscope is shown clearly in two cases which I have had within the past year. Two children, one 18 months and the other 2 years of age, each had a polyp from 1.5 to 2 cm. in diameter. On removal and section, they showed adenocarcinoma grade I. In one of these, to date, the tumor has not returned. In the other one there is another tumor of about the same size that has developed on the opposite side of the rectum. If children 2 years of age or less have adenocarcinoma, certainly it behooves us to consider other tumors in older persons as precancerous tumors, and therefore they should be sectioned and studied.

DR. EDWARD G. MARTIN, Detroit: In discussing this paper, may I add a theory in which I thoroughly believe. One must

differentiate between so-called precipitating causes of cancer and the primary etiologic factor itself. In my opinion, cancer no matter where it is found is caused by an individual susceptibility to an unknown something which as yet remains undefined; something which permits the initiation of the malignant drive. If the use of the term is not too hackneyed, call it protracted allergy. This theory lends itself reasonably to any discussion bearing on the etiology of cancer. Injury is often considered an etiologic factor in cancer of the breast, yet there are probably a thousand injuries in which no cancer develops to each one that does; the individual susceptibility, in other words, is lacking. Consider cancer in any location and the current discussion of its cause; the same reasoning applies. If smoking a pipe caused cancer of the lip or tongue without an individual susceptibility, there would be a thousand times as many cases as there are. If anal disease, such as fistula and hemorrhoids, were an important factor in the etiology of cancer, anal cancer, which is comparatively rare, should be found daily. Such work as has been presented by the authors is of the utmost importance in forming a background for the study of cancer, and without such pioneer work little would be known about cancer. The observations which have been made disclose the desirability of caring for all anal disease and more careful examination leading to such care. Statistics do not prove that cancer is hereditary, and as a matter of fact the incidence of cancer, strangely enough, has been found to be greater in the family histories of those without cancer than it has among those patients who suffer from the disease.

OSTEOMAS OF PARANASAL SINUSES AND THE MASTOID PROCESS

REPORT OF CASES

BERT E. HEMPSTEAD, M.D.
ROCHESTER, MINN.

Osteomas that arise in the paranasal sinuses are not common. Occasionally they are discovered in routine roentgenologic examination of the sinuses. They are not diagnosed clinically or even suspected of being present until either evidence of intracranial complications becomes manifest or external deformities appear. From time to time, articles have appeared that contain reports of cases and give the number of cases previously reported. It is not the purpose of this paper to give a detailed review of the literature; rather, it is to stress methods of handling cases. In 1935 Dr. Carmody reviewed the cases reported up to that time.

ETIOLOGY

The etiology of these bony growths never has been determined. The ethmoid bone is developed from cartilage and the frontal bone is developed from membrane. Osteomas develop frequently at the site of the fronto-ethmoidal suture. Arnold¹ advanced the hypothesis that cartilaginous rests were present and that these enlarge and develop later into bone. He pointed out that where tissues of different embryologic origin come together there is a predisposition to growth of tumors.

Against this hypothesis is the fact that no cartilaginous debris ever has been found in these tumors and that tumors appear at sites where this difference in embryologic derivation does not exist, such as at the recessus nasalis of the frontal bone, at the maxillary antrum and at the tip of the mastoid bone. Virchow¹

believed that the site of origin of such tumors is the diploe of the frontal bone. Scarcely would this explain occurrence of the growth in other places. Infection has been suggested as a possible cause, but many times the tumor is present without any evidence of infection, either macroscopic or microscopic. A history of trauma is obtained many times. The blow, however, usually is so insignificant that probably it is not the etiologic factor. Bornhaupt¹ advanced the hypothesis that such tumors originate from the periosteum.

PATHOLOGY

These tumors may be hard and eburnated in structure, they may be spongy, or they may consist of a mixture of these two types of structure. Growth is very slow. Usually the tumor is attached by a pedicle of cancellous structure. This growth can prevent drainage of the sinus and thus can give rise to a pyocele or mucocoele, which may be the direct cause of deformity.

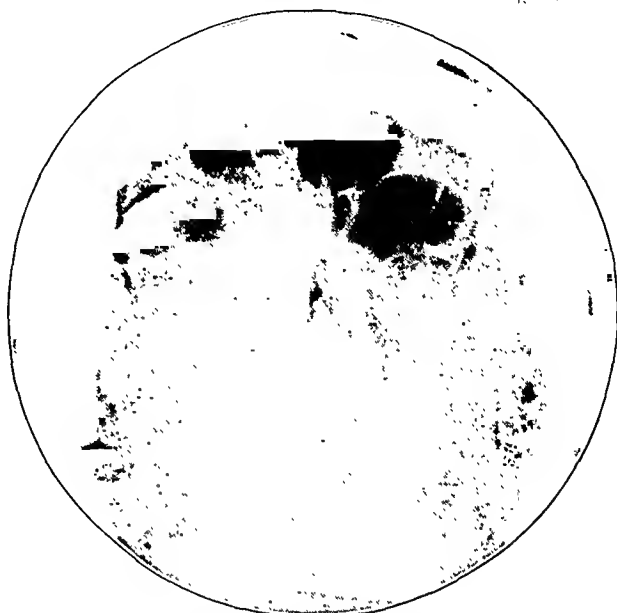


Fig. 1 (case 1).—Osteoma in ethmoid region before operation.

DIAGNOSIS

The small osteoma which elicits no symptoms is discovered only in routine roentgenologic examination of the paranasal sinuses. This type of osteoma should be reexamined subsequently at periodic intervals and, if any evidence of growth appears, should be removed.

The patient who has an osteoma usually presents himself because of pain, external deformity or symptoms due to an intracranial complication. Roentgenologic examination is of the greatest service in indicating the exact site of the tumor and whether or not it has invaded the cranial cavity. This point must be determined carefully by stereoscopic examination, since the surgical approach depends much on this. Presence of pyocele or mucocoele cannot be determined always preoperatively because the results of examination of the nose can be negative. If the nasofrontal duct is occluded, conditions are ideal for development of either pyocele or mucocoele.

OPERATIVE REMOVAL

Cushing² in 1927 reported four cases in which osteoma of the fronto-ethmoidal region occurred, with

From the Section on Otolaryngology and Rhinology, the Mayo Clinic. Read before the Section on Laryngology, Otolaryngology and Rhinology at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 15, 1938.

1. Quoted by Armitage, George: Osteoma of the Frontal Sinus, with Particular Reference to Its Intracranial Complications and with the Report of a Case, *Brit. J. Surg.* 18: 565-580 (April) 1931.

2. Cushing, Harvey: Experiences with Orbito-Ethmoidal Osteomata Having Intracranial Complications, *Surg., Gynec. & Obst.* 44: 721-742 (June) 1927.

intracranial complications. Operation in all was performed by use of an osteoplastic flap which allowed exposure of the tumor from above. In each instance the osteoma had pushed the dura ahead of it and it was not possible to separate the dura from the tumor without producing a tear. Two of these patients died of meningitis. The other two patients were benefited by use of a fascial stamp taken from fascia lata and



Fig. 2 (case 1).—Osteoma removed from ethmoid.

placed over the tear in the dura. This prevented occurrence of cerebrospinal rhinorrhea with subsequent meningitis. Cushing called attention to the fact that removal of such osteomas is a serious operation and that the ophthalmologist, the neurosurgeon and the rhinologist should consult and decide on the best method of approach. He said that there could

be no more permanence to the boundaries of a surgical specialty than there could be to the boundaries of the Balkan states.

He is undoubtedly correct in stating that if a tear is likely to occur in the dura owing to separation of it from the tumor or if a tear already is evidenced by presence of pneumatocele or other intracranial complication, surgical approach should be from above. Harris³ and Carmody,⁴ however, reported cases of a like tumor associated with cerebral extension of the lesion; the tumor was removed successfully by use of the usual incision for the fronto-ethmoidal type of operation.

Presence of infection in the frontal or ethmoidal sinus makes the approach used by Cushing much more hazardous, as meningitis or infection and subsequent loss of the bone flap may occur. In view of the fact that most often an associated sinusitis is present, it seems to me that the usual fronto-ethmoidal approach will not only permit removal of the tumor but also assist adequate handling of the infection. If, in the course of operation, it becomes evident that there is danger of tearing the dura, operation can be stopped after thorough drainage has been established and after the sinusitis has been cared for; the tumor can be removed at some future time by the method used by Cushing.

Most osteomas are not associated with extension of the lesion to the cerebrum and can be removed through the fronto-ethmoidal incision.

CONCLUSIONS

1. Osteomas of the paranasal sinuses are not common.
2. Most osteomas can be removed through the fronto-ethmoidal incision.
3. If osteomas do not involve the dura or cribriform plate, removal by the method of Cushing is illogical.

3. Harris, Robin: Osteoma of the Frontal Sinus: Report of Two Cases, *Laryngoscope* 38: 331-346 (May) 1928.
4. Carmody, T. E.: Osteoma of the Nasal Accessory Sinuses, *Ann. Otol., Rhin. & Laryn.* 44: 626-643 (Sept.) 1935.

4. Pyocele or mucocele of the sinuses can be handled best through the fronto-ethmoidal incision.

5. Osteomas associated with intracranial complications are cared for best through the transfrontal approach.

6. If osteomas are associated with intracranial complications and with definite infection of the sinuses, operation might be done in two stages with advantage.

REPORT OF CASES

CASE 1.—A youth aged 17 years came to the clinic Jan. 7, 1935, complaining of bulging of the left eye, epiphora and pain in the orbit. Bulging had been noticed for three weeks, pain for about three months and epiphora for five months. There had been no intranasal symptoms. His general health had been good. Vision and visual fields of both eyes were normal. The left eye protruded downward and outward.

Röntgenologic examination gave evidence of the presence of a large tumor, apparently of bone, that filled the left ethmoidal region and protruded into the left orbit (fig. 1). The bony mass also could be palpated with a probe in the left middle meatus.

January 12, operation was performed under intratracheal anesthesia. The incision was made in the left brow and was extended down the side of the nose. The periosteum was retracted and the tumor was found presenting at the region of the inner canthus. The tumor was of such density that it could not be removed in pieces. The os planum and parts of the lacrimal, nasal and superior maxillary bones were removed. The osteoma was then grasped with a rongeur, was rocked from its bed and was delivered entire. The growth measured 4.5 by 4 by 2.5 cm. (fig. 2). The wound was closed. Convalescence was uneventful. The patient was dismissed on January 26, at which time the wound was healed. The diplopia,

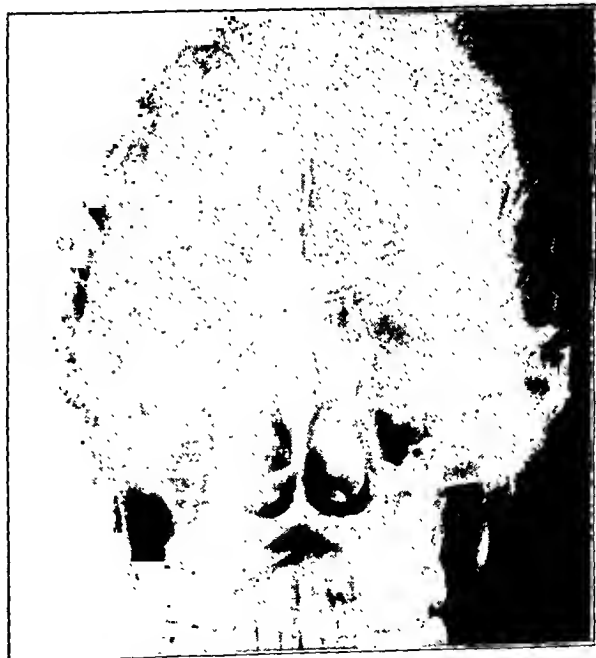


Fig. 3 (case 1).—Appearance after removal of osteoma from ethmoidal region.

which had developed postoperatively, had disappeared and the eye was in its normal position, the exophthalmos having disappeared (fig. 3).

In case 2 a large osteoma was situated on the mastoid process. This is the only case ever seen at the clinic and I can find no similar case reported in the literature in English. Several cases, however, have been reported in the German literature.

CASE 2.—A woman aged 22 consulted us at the clinic on Feb. 27, 1928, because of pain behind the left ear. She gave

the history of discharge from this ear six years previously; the discharge ceased in a few days. The discharge did not recur but, four months before she came to the clinic, she had noticed a mass behind the left ear and some pain. Examination gave evidence of a normal membrana tympani and normal hearing. There was a hard, firm mass, about 2 cm. in diameter,

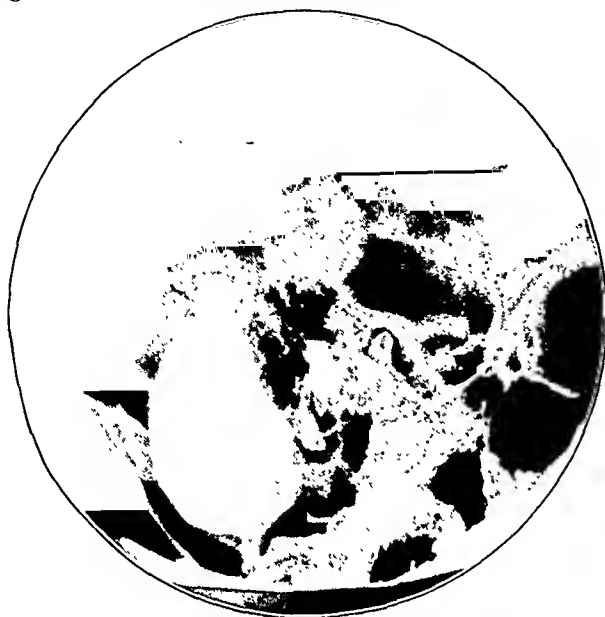


Fig. 4 (case 2).—Osteoma of mastoid before operation.

lying over the tip of the mastoid prominence. Roentgenologic examination gave evidence that this was an osteoma. Surgical removal was not advised (fig. 4).

The patient returned to the clinic May 6, 1929, and stated that she had experienced no trouble with the ear since her last visit. She again returned Jan. 7, 1935, because of abdominal pain. She was referred to the Section on Otolaryngology and it was noted that the tumor was enlarged markedly. Roentgenologic examination gave evidence that the mastoid cells were not involved. The patient was desirous of having this tumor removed because of its size.

Under general anesthesia the growth was removed and it was found attached to the tip of the mastoid. This attachment was cut through with a chisel and the growth, measuring 6.5 by 5 by 3.5 cm., was removed (fig. 5). The bone along the attachment was removed in order to prevent recurrence. The wound healed by primary union.

The pain complained of by this patient was not caused by the osteoma but by an unerupted wisdom tooth. This was removed.

ABSTRACT OF DISCUSSION

DR. GEORGE H. WILLCUTT, San Rafael, Calif.: The subject of osteoma of the paranasal sinuses is of interest because many of us who are not associated with the larger clinics and hospitals don't see many of these cases. In 1935 in Toronto Dr. Carmody reported a number of cases of osteoma of the frontal sinus and also included some of the antrum. Dr. Carmody had attacked those also by the direct method rather than by the upper or more complicated method of Dr. Cushing. Osteomas arising in this region are not common. In the last decade more cases have been reported, possibly because of more careful diagnosis. A differential diagnosis is sometimes difficult unless microscopic examination of the tissue removed is done. Most writers seem to agree that the etiology of these growths is debatable. Dr. Hempstead outlined well the various theories and hypotheses of Arnold and Bornhaupt and Virchow and others. The technic of Dr. Harvey Cushing, which he presented in 1927, was to attack these cases from above, making a big osteoplastic flap. He stressed the dangers and the seriousness of such a procedure and it rather discouraged the average operator from attacking the condition. Dr. Hempstead advances

the idea that a much more simple method is feasible. The osteoma isn't the bugbear that it appeared to be from Dr. Cushing's point of view. Naturally, if one should run into a case of extension into the cranial cavity, it might be more difficult to attack it by this method, but one could do the first step of the operation and then at a later date go in from above, or one could get somebody else to go in from above who was more familiar with that technic. It is a revelation to find that this tumor can be attacked by the average man without the necessity of becoming an intracranial surgeon. Dr. Hempstead's mastoid osteoma case is extremely interesting. I was unable to find any reference to a similar case in American or English literature.

DR. THOMAS E. CARMODY, Denver: I don't know anything about osteomas of the mastoid because I have never seen one, nor did I see anything in the literature about it. Osteomas, like other conditions, may come all at once. Of the four that I reported of the frontal sinus (I also reported two of the maxillary sinus at that time), two came within two weeks and the other two came within two years (all of them came within two years), so one might run across many of them in a short time or one may not see any for several years. I had seen only one before in twenty-five years of practice. Dr. Hempstead's idea of the technic of the operation is the same as mine. I do not think it necessary to make a great operation of this, even though the cranial cavity has been invaded. In two of my cases the cranial cavity had been invaded. In one it gave no symptoms. In the other it gave marked symptoms, because the patient had an aphasia and paralysis of the arm and leg on the right side. This cleared up after operation but the man had an epileptic attack. There is a possibility in opening through the nasofrontal duct, because it was also involved with the orbit and the ethmoid, that the entrance of air and water was possible. There is a possibility that there was some pressure on the brain or on the dura in this case. Another patient had epilepsy before the tumor was removed. There was only a slight opening in the posterior wall of the sinus in this case, and the epilepsy was not relieved by removal of the tumor. Since my report, I have found twenty-two cases in the literature—fourteen frontals, two ethmoids, five maxillaries, and one involving the maxillary and frontal sinuses. There are a great many of these cases seen that have not been reported.



Fig. 5 (case 2).—Osteoma removed from mastoid process.

DR. HARRINGTON B. GRAHAM, San Francisco: I had occasion recently to see a patient with an extremely large tumor involving both frontal sinuses. The interesting part of this case is that I saw him in 1931. Comparing his roentgenograms at that time with those of the present affords a definite idea of the rapidity of growth of one of these tumors. The lesion at that time appears to have been about one fifth the size of the present growth. The difficulty in operating in these cases has been described by the author. In my case only one thing could be done and that was to remove the anterior wall of the frontal sinus. This wall proved to be very thin and was easily dis-

posed of. The tumor was discrete but was so large that it compelled me to divide it into two parts by chiseling through the center. After one half of the tumor had been removed it was possible to elevate the other half without injuring the posterior wall of the sinus. There were three distinct tumors lying in the left orbit which were not connected with the mother growth and I find from the literature that this is not an unusual condition; these separate tumors seemingly have their own blood supply and are found frequently in the soft tissues. Since Dr. Carnody's work there have been a good many cases added to the literature, especially from Hungary, where considerable work has been done on the pathology.

PATHOLOGIC CHANGES IN AMBLYOPIA FOLLOWING TRYPARSAMIDE THERAPY

P. J. LEINFELDER, M.D.

IOWA CITY

The pentavalent arsenical atoxyl, introduced in 1902 by Blumenthal,¹ was first used in the treatment of protozoan diseases in 1905 by Thomas.² Since, as the name indicates, the drug was considered nontoxic, it was used extensively in the therapy of trypanosomiasis, pernicious anemia and psoriasis. After the identification of *Spirochaeta pallida*, the drug was almost immediately applied to the treatment of syphilis. Extensive use of atoxyl soon demonstrated various cases of toxicity. Progressive loss of vision occurred frequently (Bornemann,³ Igersheimer,⁴ Beek,⁵ Fehr⁶), and studies of the visual fields showed that the subjective blurring of vision was accompanied by peripheral contraction that progressed to complete blindness. Once visual symptoms occurred, visual loss continued in spite of withdrawal of the drug. Loss of vision developed in nonsyphilitic as well as syphilitic patients, and it appeared that the drug acted specifically on the visual sensory mechanism.

In 1907 Ehrlich's⁷ studies in chemotherapy led to the discovery of arsacetin, a less toxic substitution product of atoxyl. The new drug was used only a short time, since clinical experience demonstrated that it also had a deleterious effect on vision (Sattler,⁸ Hammes,⁹ Iversen,¹⁰ Ruete¹¹). The hope for a non-toxic pentavalent arsenical led to the introduction of tryparsamide by Lorenz and Loevenhardt.¹² Once more clinical application showed that the new drug, although less toxic than atoxyl or arsacetin, also caused

deterioration of vision and optic atrophy (Woods and Moore,¹³ Neff,¹⁴ Cady and Alvis,¹⁵ Fine and Barkan,¹⁶ Mayer¹⁷). With tryparsamide, however, visual injury was less common, and improvement or at least a cessation of the toxic process occurred when administration of the drug was discontinued. Recent reports have adequately reviewed the clinical use and toxicity of tryparsamide.

Although the toxicity of the pentavalent arsenicals has been investigated by a number of authors, no satisfactory explanation for the visual pathologic changes has been determined. The toxic action of atoxyl, arsacetin and tryparsamide appears to have a special affinity for the visual system, for general symptoms most frequently do not accompany the ocular manifestations. Young and Loevenhardt,¹⁸ after experimental comparison, concluded that the aniline group in the ortho position contribute to the toxic effects of these compounds and that the pentavalent arsenic is only a secondary consideration. An indication that the visual loss is not due to arsenic or the aniline molecule of the drugs is that these substances when toxic to the visual system ordinarily cause a defect in the central field, while atoxyl and tryparsamide almost invariably cause concentric contraction of the visual fields. Furthermore, the disintegration of pentavalent arseni-

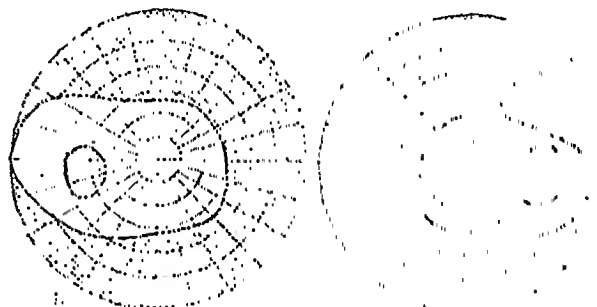


Fig. 1.—Visual fields taken prior to injection of tryparsamide; 2/1,200 tangent screen.

eals in the blood stream is very slow. From a quantity of the drug injected, arsenic is gradually split off; some of the drug remains (Igersheimer and Rothman¹⁹) in the blood and tissues, while a large portion is excreted unchanged in the urine. Young and Muehlenberger²⁰ considered the possibility of accumulation of tryparsamide as the cause of toxic effects. Igersheimer⁴ expressed the opinion that atoxyl itself or a reduction product of it acts directly on the cell. He stated also that the eye has a high affinity for the atoxyl molecule but not for arsenic. According to Meyer and Gottlieb²¹ arsenic can be demonstrated in animal eyes after poisoning with atoxyl but it cannot be identified after poisoning with arsenic. In their experiments the arsenic poisoning did not cause blindness. Osborne²²

13. Woods, A. C., and Moore, J. E.: Visual Disturbances Produced by Tryparsamide, *J. A. M. A.* 82:2105 (June 28) 1924.

14. Neff, E. E.: Effect of Tryparsamide on the Optic Tract: A Chemical Study, *Wisconsin M. J.* 24:569 (Aug.) 1925.

15. Cady, L. D., and Alvis, B. Y.: The Uses of Tryparsamide in Patients With and Without Ocular Lesions, *J. A. M. A.* 80:184 (Jan. 16) 1926.

16. Fine, Max, and Barkan, Hans: Prevention of Ocular Complications in Tryparsamide Therapy, *Am. J. Ophth.* 20:45 (Jan.) 1937.

17. Mayer, Leo L.: Tryparsamide Therapy of Neurosyphilis and Atrophy of the Optic Nerve, *J. A. M. A.* 109:1793 (Nov. 27) 1937.

18. Young, A. G., and Loevenhardt, A. S.: The Relation of the Chemical Constitution of Certain Organic Arsenical Compounds to Their Action on the Optic Tract, *J. Pharmacol. & Exper. Therap.* 23:107 (March) 1924.

19. Igersheimer and Rothman, quoted by Meyer and Gottlieb,¹ p. 566.

20. Young, A. G., and Muehlenberger, C. W.: The Excretion of Tryparsamide, *J. Pharmacol. & Exper. Therap.* 23:461 (July) 1924.

21. Meyer and Gottlieb,² p. 566.

22. Osborne, E. D., Putnam, E. D., and Hitchcock, B. S.: The Effect of Arsenic on Rabbits, *Arch. Dermat. & Syph.* 25:419 (March) 1932.

From the Department of Ophthalmology, State University of Iowa College of Medicine.

Read before the Section on Ophthalmology at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 15, 1938.

1. Blumenthal, quoted by Meyer, H. H., and Gottlieb, R.: *Experimental Pharmacology*, translated by V. E. Henderson, Philadelphia, J. B. Lippincott Company, 1926, p. 565.

2. Thomas, H. W.: Some Experiments in the Treatment of Trypanosomiasis, *Brit. M. J.* 1:1140, 1905.

3. Bornemann, W.: Ein Fall von Erblindung nach Atoxylinjektionen bei Lichenrubrum, *München. med. Wchnschr.* 52:1043, 1905.

4. Igersheimer: Ueber die Wirkung des Atoxyls auf das Auge, *Arch. f. Ophth.* 71:379, 1909.

5. Beek, Max: Ueber schädigung bei Schlafkranken in Verlauf der Atoxyl, *Augenh.* 33:129, 1909.

6. Fehr, Paul: Ueber schädigung bei Schlafkranken in Verlauf der Atoxyl, *Deutsche med. Wchnschr.* 34:341, 1907.

7. Ehrlich, Paul: Chemotherapeutische Trypanosomen Studien, *Berl. klin. Wchnschr.* 44:341, 1907.

8. Sattler, C. H.: Pathologisch-anatomische Untersuchung eines Falles von Erblindung nach Arsacetininjektionen, *Arch. f. Ophth.* 51:546, 1912.

9. Hammes, F.: Zur Beurteilung des Arsacetins und seiner Einwirkung auf den Sehnerven, *Deutsche med. Wchnschr.* 36:267, 1910.

10. Iversen, J.: Ueber die Behandlung russischen Recurrens mit Arsacetin, *München. med. Wchnschr.* 56:1785, 1909.

11. Ruete: Ein Fall von Sehnervenerkrankung nach Arsacetininjektionen, *München. med. Wchnschr.* 56:718, 1909.

12. Lorenz, W. F., and Loevenhardt, A. S.: The Therapeutic Use of Tryparsamide in Neurosyphilis, *J. A. M. A.* 80:1497 (May 26) 1923.

showed that arsenic in moderate amounts can be identified in the rabbit brain after therapeutic doses of tryparsamide.

Although numerous cases of tryparsamide amblyopia have been observed clinically there have appeared no reports of histologic examination of the eyes and optic pathways in such cases. Reports of pathologic changes in amblyopia following the use of atoxyl were made by Nonne²³ and Birch-Hirschfeld²⁴ and following the use of arsacetin by Sattler.⁵ Nonne observed atrophy in the optic nerves, chiasma and tracts obtained from a patient who died several weeks after blindness occurred. A clinical recognition of optic atrophy had been made before death. In Birch-Hirschfeld's case a complete examination was made of a man who died two years after the beginning of administration of atoxyl and twenty-two months after complete loss of vision. The atoxyl was used in the treatment of psoriasis. His study disclosed degeneration of the third neuron, chromatolysis, disintegration of the retinal ganglion cells and gliosis of the retina. Some nuclei of the inner nuclear layer appeared faded. The peripheral portion of the outer nuclear layer contained many shrunken nuclei. There was almost total degeneration of the optic nerves but no evidence of inflammation. The ganglion cells of the lateral geniculate bodies also showed degeneration. After injection of atoxyl in experimental animals Birch-Hirschfeld²⁴ was able to demonstrate a similar condition. Changes in retinal ganglion cells were observed in the cat, and extensive chromatolysis was observed as early as nine and one-half days after injection in a dog. In some dogs he observed changes in the occipital cortex and geniculate bodies. He said that the retina was most susceptible to the poison but that the condition behaved like a purely degenerative process of the medullary sheaths of the optic nerves. Sattler described the pathologic changes in a case of amblyopia following treatment of pernicious anemia with arsacetin. Loss of vision began six weeks after the beginning of treatment and progressed to total blindness in an additional six weeks. Death occurred five weeks later. There were no demonstrable changes in the first neuron, but a shrinkage or a swelling of a few cells in the inner nuclear layer was seen. The greatest damage was to the retinal ganglion cell layer and the optic nerve. Gliosis and reduction in the number of the ganglion cells were reported. The ganglion cell nuclei were shrunken or had lost their sharp margins, and the Nissl substance was not visible. The greatest degree of myelin disintegration occurred in the anterior portion of the optic pathway. More recently Sattler²⁵ expressed the opinion that although one would expect the process to be primary in the retina it is possible that the processes in the nerve fiber and the retina advance at the same time. A striking fact concerning all the reports of pathologic changes is the absence of evidence of tissue changes outside the eye and the optic pathways, for the remainder of the organs and the central nervous system show no evidence of a related pathologic process.

These observations of the pathologic changes in amblyopia occurring after the administration of compounds containing pentavalent arsenic were made at a time remote from the onset of blindness. A complete study of a case in which pathologic material was

obtained nine days after the administration of 1 Gm. of tryparsamide and seven days after the onset of visual disturbances is presented:

A white man aged 52 was admitted Aug. 13, 1937, because of inability to walk. This manifestation, together with difficulty in control of the bladder, had begun two years previously. There was a history of gonorrhea in 1907. The examination showed 6/6 vision in each eye. The pupils were round and equal and reacted promptly and effectively in near accommodation, but the reaction to light was sluggish. Ophthalmoscopic examination revealed early optic atrophy of the primary type on both sides; the visual fields (fig. 1) showed contraction with a 2/1,200 mm. target on the tangent screen. The blood pressure was 140 systolic and 86 diastolic, there was a cord bladder, the patient was unable to walk and the Wassermann reactions of the spinal fluid and blood were 4 plus.

On August 16, 1 Gm. of tryparsamide was administered intravenously. On the morning of August 18 a cystoscopic examination was made and was followed by chills, vomiting and fever, the temperature reaching 103 F. During the afternoon of that day the patient complained of blurring of vision. The following morning there was no subjective central or peripheral vision, but the pupils responded sluggishly to light, as at the time of admission. The ophthalmoscope revealed no

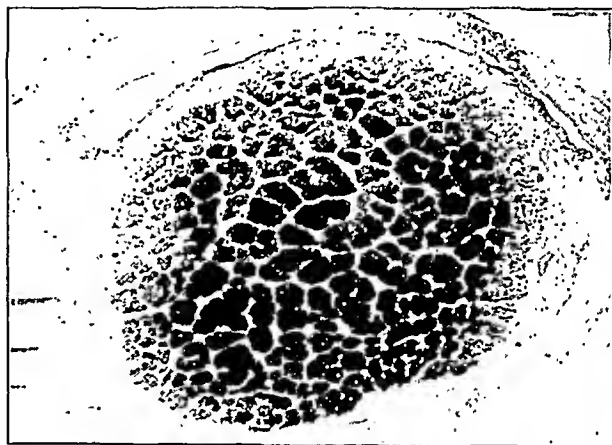


Fig. 2.—Optic nerve. Old peripheral degeneration is evident; Held stain.

change in the appearance of the nerve heads or fundi. On August 20 blindness persisted, but no pupillary response to light could be elicited. The pupils were smaller than at previous examinations. The general condition of the patient failed progressively. Further external examination of the eyes disclosed no pupillary light reaction, and no new changes developed in the fundus. The urea nitrogen content rose to 130.9 with a creatinine content of 11.5, and death from uremia occurred on the morning of August 25. A complete necropsy was begun two hours after death.

General pathologic examination was made by Dr. H. P. Smith, head of the department of pathology. He reported that the liver showed no evidence of necrosis. The cells in the central part of each lobule showed fat droplets and fine brown pigment granules. The kidneys were markedly reduced in size (weighing 90 Gm. each), but the renal pelvises were distended. Histologically there were extreme changes of a chronic nature that had destroyed the tubules and hyalinized the glomeruli. The stroma between the tubules was involved in an extensive chronic inflammatory process. Although the pathologic changes were compatible with those of chronic nephritis, the inflammation and dilatation of the renal pelvises indicated the presence of pyelonephritis. There was no evidence of acute change. The pathologist believed that the patient had been on the verge of uremia for some time and that very little additional injury was necessary to bring about a critical change. Additional postmortem diagnoses were bronchopneumonia and meningovascular syphilis.

23. Nonne, M.: Anatomische Untersuchung eines Falles von Atoxylblindung, *Med. Klin.*, 4: 757, 1908.

24. Birch-Hirschfeld, A., and Koster, G.: Die Schädigung des Auges durch Atoxyl, *Arch. f. Ophth.* 76: 403, 1910.

25. Sattler, C. H., in Schieck, F., and Brückner, A.: *Kurzes Handbuch der Ophthalmologie*, Berlin, Julius Springer, 1932, vol. 7, p. 251.

The posterior segment of each eye was fixed in absolute alcohol and acetic acid according to Nissl's technic for study of the retinal ganglion cells. Pieces of the nerves and tracts were fixed in osmic acid, Marchi, and solution of formaldehyde for hematoxylin and eosin, silver, and Held stains. Portions of the occipital cortex and the lateral geniculate bodies were placed in 10 per cent solution of formaldehyde in preparation for hematoxylin and eosin, and Nissl stains.

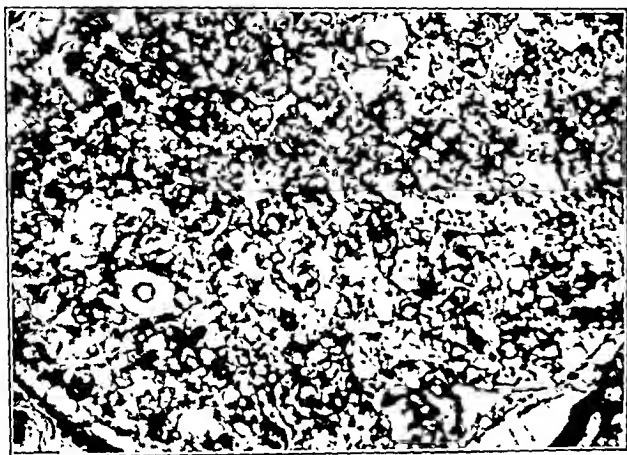


Fig. 3.—High power view of normal medullary sheaths of optic nerve; osmic acid stain.

The occipital cortex and the lateral geniculate bodies showed no evidence of injury to the cell bodies, and the topography of the regions was normal. There was neither chromatolysis nor disturbance of the nuclei. Fatty granules were observed in the cytoplasm of the cells of the lateral geniculate body and other regions, but these changes are considered physiologic in a person of this age.

The optic tracts posteriorly showed little evidence of change with the Held stain. Small areas of gliosis indicated the presence of an old atrophic process, but the osmic acid and Marchi preparations revealed no evidence of acute demyelinating disease. In the anterior portion of the optic tracts the changes were similar but the amount of gliosis was more definite. Staining of the axis cylinders with silver proved them to be intact.

The periphery of both optic nerves showed gliosis and old disintegration of the myelin sheaths that appeared in proportion to the visual field changes (fig. 2). No areas of inflammatory reaction were observed, and the nerve sheaths were of normal appearance. Osmic acid (fig. 3) and Marchi preparations showed no evidence of acute degeneration in the optic nerves.

Within the retina there was gliosis in the nerve head and retina consistent with the antemortem diagnosis of early optic atrophy. Low power microscopic examination of the retina showed a normal morphologic appearance, with the several layers distinctly discernible. Ganglion cells were present in abundance. Examination with the high power objective disclosed the rods and cones in a good state of preservation. The rod and cone nuclei appeared entirely normal. In the posterior segment of the eye the cells of the inner nuclear layer were for the most part normal, but in places cells of the innermost row appeared faded and almost homogeneous (fig. 4). The general nuclear morphologic appearance could be made out, but no evidence of a chromatin network or of cytoplasmic structure could be recognized. The appearance was that of ghost cells. In the central region of the globe these cells were occasionally seen, but as one passed toward the periphery their occurrence was more frequent. The ganglion cells were numerous, but the morphologic appearance was profoundly changed (fig. 5). The cells were irregular in outline, and the cytoplasm in some cells was cloudy while in others it had a foamy appearance. In most of the ganglion cells the Nissl substance had entirely disappeared, but a peripheral rim of Nissl granules was recognized in a few cells. The ganglion cell nuclei were variable. Some were large, homogeneous and apparently

swollen, while in some cells a faint indication of a chromatin net remained, and a few cells contained a nucleolus. Many glial cells were present in the ganglion cell and nerve fiber layers. The nuclear changes and the loss of Nissl substance indicate a profound cellular reaction similar to that seen in the central nervous system after acute intoxications.

COMMENT

The reports of pathologic changes occurring after the use of atoxyl (Birch-Hirschfeld) and arsacetin (Sattler) show several results similar to those here reported for trypanamide. Both observers recognized changes in the ganglion cells and in the inner nuclear layer of the retina as well as degeneration of the nerve fibers of the optic nerve. In experimental work, however, Igersheimer was unable to find any evidence of change in the ganglion cells of the retina of the cat or dog, but Birch-Hirschfeld's animals showed abnormalities similar to those observed in his reported case. The pathologic state in the cases recorded differs from that in the present case, since in the previous cases the process had gone on to a chronic stage. Histologic examination immediately after administration of the pentavalent arsenicals and the development of amblyopia has not previously been reported.

The present study presents observations in agreement with previous reports in regard to the changes in the ganglion cells and in the inner nuclear layer, but evidence of acute primary degeneration of nerve fiber in the optic pathways was not present. It seems apparent that changes in the optic nerves, tracts and lateral geniculate bodies must be of a secondary nature; no evidence of acute change could be observed in these situations nine days after the administration of the drug, yet definite evidence of cellular change was observed in the ganglion cells of the retina. It seems probable that the amblyopia following the administration of trypanamide, similar to that due to tobacco and

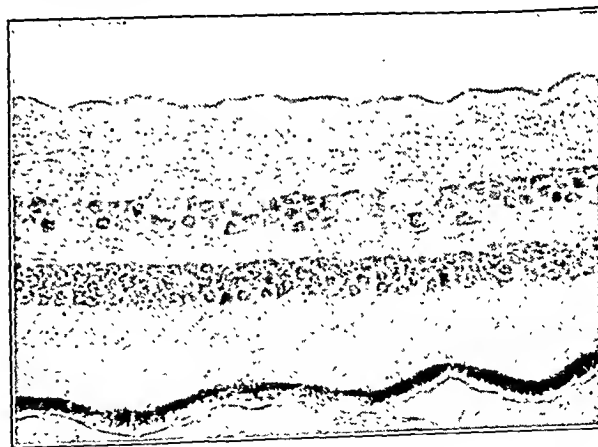


Fig. 4.—Peripheral part of retina. Two "ghost" cells are seen in the inner nuclear layer; Nissl stain.

alcohol, is caused by a primary degeneration of the ganglion cells of the retina and that there ensues a secondary degeneration of the nerve fibers and myelin sheaths. The significance of the changes in the inner nuclear layer is not known. It is possible that in less extensive injury these cells are most affected, and their degeneration results in the peripheral contraction of the visual field.

Birch-Hirschfeld expressed the opinion that arteriosclerosis or alcoholism might play a part in the causation of the condition. In this case neither of these con-

ditions was present. Accumulation of the drug has been held responsible for the pathologic changes, yet this patient received a single injection. Previous experience with tryparsamide amblyopia has demonstrated that, if ocular complications are to develop, evidence of the change usually occurs early in the treatment. In one of Birch-Hirschfeld's experimental animals extensive chromatolysis was observed nine and one-half days after the beginning of treatment, and the author ventured the opinion that the animal was idiosyncratic to the drug. Lillie²⁶ suggested an idiosyncrasy as the underlying cause of the amblyopia. The fact that the patient reported had extensive changes after a single injection of 1 Gm. of tryparsamide lends credence to this view.

SUMMARY

1. Acute degeneration of the retinal ganglion cells was observed nine days after injection of 1 Gm. of tryparsamide and seven days after the onset of blindness.
2. Acute degeneration of cells in the innermost portion of the inner nuclear layer was present.
3. Evidence of acute primary degeneration in the optic nerves and tracts was not present.
4. General pathologic changes due to arsenic poisoning were not observed.

ABSTRACT OF DISCUSSION

DR. FREDERICK C. CORDES, San Francisco: Dr. Leinfelder's report is the first histologic study of tryparsamide amblyopia. Certain observations were rather striking. The changes in the ganglion cells and innermost layers of the inner nuclear layer were very definite, especially in the periphery of the retina. The fact that the neuro-epithelial layer was not involved was also noteworthy. Of particular interest was the fact that examination of the occipital cortex, lateral geniculate bodies, optic tracts and nerves failed to reveal any evidence of acute inflammation or degeneration. The changes present in the optic nerve were those of an old process, easily accounted for by the preexisting optic atrophy. The changes noted in the retina have been observed in acute poisoning from methyl alcohol, ethyl alcohol, quinine, nicotine and atoxyl. Lillie and others have contended that the occasional cases of tryparsamide amblyopia reported have been primarily the result of idiosyncrasy to the drug. The fact that 1 Gm. of the drug produced such marked changes would tend to confirm this opinion. Clinical observation has shown that, aside from the subjective symptoms, the earliest changes are those of contracted field and not visible changes in the optic disk. The fact that the greatest changes were found in the periphery of the retina and that no acute changes were found in the optic nerve emphasizes the importance of careful field studies early in the course of therapy. The greatest controversy in tryparsamide therapy has centered around its use in the presence of optic atrophy. Last year Dr. Mayer presented a paper before this section on tryparsamide therapy which bore out his contention that tryparsamide was not contraindicated in optic atrophy. Dr. Leinfelder's report seems to confirm this. If the effect of tryparsamide in a sensitive person was primarily on the optic nerve and tracts, one would expect to find signs of acute degeneration or inflammation in these structures, especially in view of the fact that the eye was examined so soon after administration of the drug. Lorenz and Loevenhardt, in introducing the drug, warned against its use "in cases showing degenerative changes in the retina." The fact that the acute changes in the histologic report presented were limited to the retina should make us extremely cautious in advising the use of the drug in the presence of pathologic changes in the retina. Dr. Leinfelder's paper is an important contribution to the subject of tryparsamide therapy.

DR. MAX FINE, San Francisco: It is unfortunate that the picture was somewhat confused by the presence of an early optic atrophy in Dr. Leinfelder's patient. There is general agreement, however, that tabetic optic atrophy begins in the intracranial portions of the optic nerve. The absence of extensive atrophy in the optic nerves in the presence of marked degenerative changes in the ganglion cell and inner nuclear layers suggests that the process involved is one other than tabetic optic atrophy. A striking feature of the sections Dr. Leinfelder has exhibited is the relative integrity of the central portion of the retina and the progressively severe changes as the periphery is approached. These observations correspond in a rough manner to the peripheral constriction of the visual field in cases of tryparsamide amblyopia. The delayed appearance of optic atrophy in tryparsamide amblyopia, even when the field changes are severe, fits in with Dr. Leinfelder's conclusion that the degeneration occurs first in the inner nuclear layer. The ocular complications from tryparsamide may be divided for clinical purposes into two groups: One shows the usual reaction consisting of preliminary symptoms of blurring, followed by a depression of the peripheral field with relative sparing of the temporal field. The process is reversible if tryparsamide is discontinued early, when the field changes are not too far advanced. The second type of reaction, of more infrequent occurrence, is an acute intoxication in which the patient may go to complete blindness within forty-eight hours

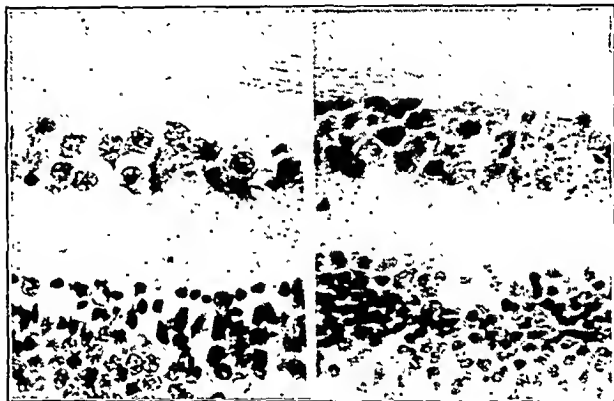


Fig. 5.—Normal retina and ganglion cells are shown on the left. Acute degeneration of ganglion cells of the retina after injection of tryparsamide is seen on the right; Nissl stain.

after a single injection of tryparsamide. This reaction is much less reversible. There may be a degree of recovery, but usually there is severe permanent damage. I have seen three such patients who became almost totally blind after the first or second injection of tryparsamide. Each of these patients had an early primary optic atrophy before the institution of tryparsamide therapy. Dr. Leinfelder's case appears to fall into this group. The occurrence of more than 90 per cent of reactions with the first five injections speaks against a cumulative effect in the ordinary sense. Young and Meuhlenberger have shown through studies of urinary arsenic that whereas a great majority of persons excrete 95 per cent of the arsenic within twenty-four hours, a small number excrete the drug much more slowly, and in one instance arsenic was recovered from the urine after three weeks.

DR. JOHN E. WEEKS, Portland, Ore.: I have been interested in this subject because I have seen two cases of amblyopia from the use of tryparsamide. In neither was there any intimation of impairment of vision before the tryparsamide was administered. Both were cases of syphilis of long standing. In the first case three doses were given at five day intervals; the first two were small, the third a dose of 1.5 Gm. The vision on the second day after the last dose was impaired. The fundi showed almost no change. Vision of one eye was reduced to 22/100, of the other eye to 20/70. The fields of vision were narrowed concentrically in both eyes, about 15 degrees in one eye and 25 degrees in the other. The blood vessels were somewhat reduced in size. There was no exuda-

26. Lillie, W. I.: Peculiar Contraction of the Normal Fields Associated with Syphilis of the Cerebral Nervous System, *Tr. Am. Ophth. Soc.* 32: 153-163, 1934.

tion and no hemorrhage, but the temporal portions of the disks were a bit pale. Vision of 20/20 was recovered in both eyes, but moderate concentric limitation of the fields persisted. In the second case, tryparsamide had also been injected once before the second dose, from which the amblyopia followed, was given. The second dose was 1.5 Gm. given intravenously. The patient became totally blind in twenty-four hours. An ophthalmologist who examined him could not detect that he had any vision whatever. The fundi in this case were similar to the fundi in the other case. I saw the patient in the afternoon of the day of his complete blindness, at which time the right iris reacted slightly to the stimulus of light but not the left. However, within a week the vision was greatly improved and the field of vision was very much contracted. Eventually the patient obtained a field of vision of only about 20 degrees in each eye but a visual acuity of 20/20. I regard the use of tryparsamide as something that should be undertaken only after careful tests regarding the susceptibility of the patient to tryparsamide have been made. There is a widespread opinion that, wherever there is any atrophy of the optic nerve or any disturbance of the fundus from syphilis, tryparsamide should not be employed. This amblyopia corresponds to some extent to that of quinine amblyopia, but the use of tryparsamide has caused permanent total blindness in a few cases. No case of complete permanent blindness from quinine is on record.

DR. OTIS A. SHARPE, San Francisco: A man aged 25 was being treated for syphilis with tryparsamide. He was referred to me one morning for visual fields. He complained of some indefinite disturbance in the fields. I took the fields, and there was about 10 or 15 degrees concentric contraction. The vision was 20/15 in each eye. I advised discontinuance of the treatment. The next morning I was called to the ward, where it was reported that he had gone completely blind. When I first examined the background there was no visible change. The next morning, which was less than twenty-four hours, the man was completely blind; there were no changes in the backgrounds to be seen. There was a very slight reaction of the pupils to light. Five years later this man appeared in my office and wanted a report from me. I examined his eyes and the background showed perfectly white disks. He took the case to court, claiming that the tryparsamide was the cause of his blindness. The other side claimed it was syphilitic optic atrophy. I reported this because of the short time in which complete blindness developed.

DR. FREDERICK H. VERHOEFF, Boston: At the present time it seems to me to be of no practical importance whether tryparsamide or other arsenicals in producing blindness affect primarily the optic nerve or the retinal ganglion cells, but of course the question is of great scientific interest and may become of practical importance. I haven't the slightest doubt that Dr. Leinfelder has shown in this case that the ganglion cells were markedly affected, but I do not feel sure that they were primarily affected. It seems to me, in spite of the fact that histologically there was no evidence that the nerve fibers were affected, that it was perfectly possible that they may have been affected to such an extent as to produce changes in the ganglion cells. This question has arisen in connection with many toxic agents and in my opinion has seldom if ever been satisfactorily answered.

DR. EDWARD JACKSON, Denver: Bearing on the point that has been brought up by Dr. Verhoeff, many years ago I was consulted by a young man with very marked macular changes. There were some slight hemorrhages and a good deal of haziness in the macula. One of the first questions I asked him was whether there was any history of blindness or partial blindness in his family. He stated that absolutely there had been none; but two years after that Dr. George M. Gould, who knew the family, reported it as a case of Leber's disease, which without any doubt it was. I saw it at a very early stage, and the appearance of the retina seemed to point out what one would expect, that the nutrition of the ganglion cells in the macula was affected before the nerve fibers proceeding from that cell showed any sign of change. There was no signs at first of disease in the optic disks. It ran the course of Leber's disease.

DR. P. J. LEINFELDER, Iowa City: Dr. Verhoeff's question concerning whether the ganglion cells were primarily affected or the nerve fibers I think can be definitely answered. Although neurohistologic technique is by no means infallible, research that I have done with the optic nerve has shown conclusively that, if one sections or injures the optic nerve, pathologic changes are observable with the osmic acid and the Marchi methods as early as three days following the injury. Furthermore, the neurofibrils show disintegration within ten days. I think it is striking that in this case there were absolutely no evidences of acute degeneration in the nerve fiber of the optic nerve even close to the eyeball. Dr. Sharpe mentioned pupillary reactions. It is conspicuous in the literature that pupillary reactions are at first retained in spite of the subjective blindness. Dr. Weeks brings up two questions. One is whether the fundus was changed. I did not mention it in my primary discussion but, throughout the nine days following the injection of the tryparsamide, no changes in the fundus over those that were first observed were noted. There was no change whatever from the optic atrophy. As for patients who recover their vision, it is astounding to note the amount of reversible change that can occur in the ganglion cells of the retina following injury to the optic nerve or tracts. Extensive chromatolysis of the ganglion cells in the retina occurs early, yet a large percentage of these cells recover at a later date. This was demonstrated by Birch-Hirschfeld in 1900. Dr. Fine inquires concerning histologic differences between the nasal and temporal segments of the retina. I would not attempt an evaluation of such a thing on the histologic material available for one would need to make a great many calculations that would not yield any definite, usable data.

THE GORDON TEST FOR HODGKIN'S DISEASE

A REACTION TO EOSINOPHILS

JAMES B. McNAUGHT, M.D.

SAN FRANCISCO

In 1932 Gordon¹ reported that intracerebral inoculation of rabbits and guinea pigs with suspensions of lymph nodes from patients with Hodgkin's disease was followed in several days by an encephalitic syndrome of characteristic pattern. This was typified by early muscular rigidity, progressive incoordination, ataxia and spastic paralysis of the hind limbs, accompanied by loss of weight and subnormal temperature. Tissue suspensions from patients with acute Hodgkin's disease often produced in addition to these changes retraction of the head, opisthotonos and convulsive seizures, and the animals frequently died within a few days to a month. In the less severe type of reaction the animals passed into a chronic state with marked muscular atrophy and wasting. Gordon obtained these reactions with suspensions from nineteen of twenty patients with Hodgkin's disease and with none of forty-one control suspensions. He concluded from his studies of the properties of the pathogenic agent that it was undoubtedly a virus and was the primary causative agent of Hodgkin's disease. He proposed the biologic test as a specific one for the practical diagnosis of Hodgkin's disease.

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1. (a) Gordon, M. H.: *Rose Research on Lymphadenoma: Studies on the Aetiology of Lymphadenoma*, Bristol, England, John Wright & Sons, Ltd., 1932; (b) Hodgkin's Disease: A Pathogenic Agent in the Gland and Its Application in Diagnosis, *Brit. M. J.* 1: 641 (April 15) 1933.

The Gordon test has been applied in 179 cases of Hodgkin's disease by various investigators² and found positive in 124 (69.3 per cent). In 210 of 214 control experiments (98.1 per cent), with suspensions of lymph nodes from normal patients and from patients with hyperplasia, adenitis, leukemia, tuberculosis, carcinoma and sarcoma, the test was negative. These results indicate that while the Gordon test is only 70 per cent accurate in detecting Hodgkin's disease it apparently is highly specific in distinguishing this condition from other dyscrasias of the lymph nodes.

Gordon³ persists in his belief that the causal agent of Hodgkin's disease is elementary virus bodies, and he has recently employed emulsions of his sensitized elementary bodies, recovered from the lymph nodes of patients with active Hodgkin's disease, in treating this condition. Warner⁴ reported beneficial results following the use of Gordon's sensitized emulsions in cases of early Hodgkin's disease. Other investigators⁵ have been dubious of the virus nature of the active agent in the Gordon test. They have based their skepticism on the observation that although the pathogenic agent is definitely filter passing and the disease produced in animals bears some of the characteristics of an infectious process the agent has not been cultivated in vitro nor has its passage from animal to animal been accomplished. Gordon reported that rabbits recovering from an initial paralysis were immune to a second inoculation of active material, but other investigators⁶ found such rabbits just as susceptible as the control animals.

Friedemann and Elkeles⁷ reported that intracerebral inoculation of rabbits with extracts of normal and pathologic human bone marrow, spleen and leukocytes produced a paralysis indistinguishable from that caused by the agent which Gordon discovered in glands from

patients with Hodgkin's disease. They expressed the opinion that their active agent could not possibly be a living virus since it withstood extracting treatment which no living virus or bacteria could be expected to tolerate. In support of this theory Kelser and King⁸ submitted tissues containing known neurotropic viruses of St. Louis encephalitis, equine encephalomyelitis and rabies to the extraction processes used on the leukocytic material, and in all instances the viruses were rendered inert. Friedemann suggested that the encephalitogenic agent of Hodgkin's disease and that in the spleen, bone marrow and leukocytes are of the nature of a proteolytic enzyme such as that demonstrated by Jochmann and Lockemann⁹ in 1908. The active agent was not found in all bone marrows or all specimens of pus.⁹ MacKenzie and Van Rooyen¹⁰ confirmed much of the work of Friedemann but found no relation between the proteolytic activity and the

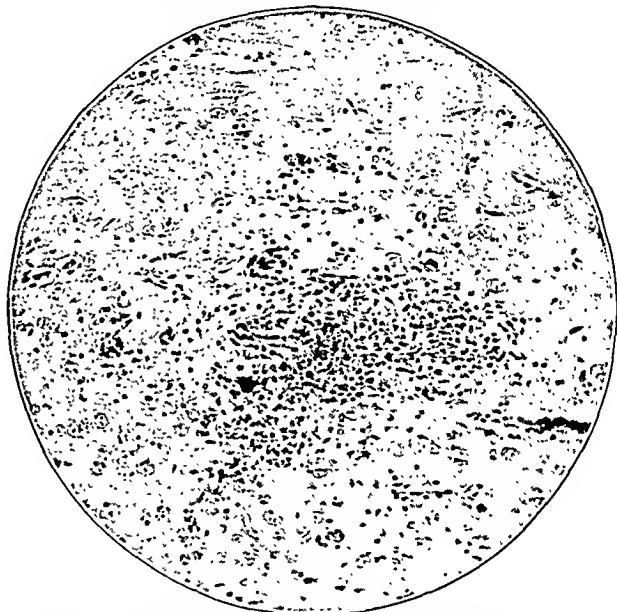


Fig. 1.—The inoculation area in the cerebral cortex of a paralyzed rabbit (slightly reduced from a photomicrograph with a magnification of 160 diameters).

encephalitogenic property of the agent and thus did not identify it with Jockmann's proteolytic enzyme.

It is obvious that, in some marrow, leukocytes, pus and spleens as well as some lymph nodes from patients with Hodgkin's disease there is an active substance capable of producing a characteristic paralysis in certain experimental animals. Turner, Jackson and Parker²ⁿ recently published convincing evidence showing that the active agents of Gordon and of Friedemann are derived from the eosinophil and consequently are most probably identical. This evidence is in accord with my observations on the Gordon test, covering a period of several years, herewith presented.

METHODS

The procedures of Gordon^{1a} have been followed in the performance of the tests. With sterile technic, human lymph nodes obtained either at biopsy or at

2. These include:
 - (a) Van Rooyen, C. E.: A Biological Test in the Diagnosis of Hodgkin's Disease, *Brit. M. J.* **1**: 644 (April 15) 1933.
 - (b) Van Rooyen, C. E.: Some Properties of the Encephalitogenic Agent in Lymphadenomatous Tissue, *Brit. M. J.* **1**: 519 (March 24) 1934.
 - (c) Van der Hoeven, J., and Hulst, L. A.: De Ziekte van Hodgkin en de Proef van Gordon, *Nederl. tijdschr. v. geneesk.* **78**: 4305, 1934.
 - (d) Dassen, R.; Fisher, A., and Fustinoni, O.: La prueba de Gordon en el diagnóstico de la linfogranulomatosis maligna, *Rev. Asoc. méd. argent.* **48**: 1397 (Dec.) 1934.
 - (e) Davis, W. B.: Hodgkin's Disease, *Brit. M. J.* **1**: 324 (Feb. 16) 1935.
 - (f) D'Ovidio, F. R., and Vucetich, Martin: Sobre un caso de enfermedad de Sternberg Hodgkin, *Rev. Asoc. méd. argent.* **49**: 372 (March) 1935.
 - (g) Manson, M. H.: Biological Phenomena in Hodgkin's Disease, *Minnesota Med.* **18**: 263 (April) 1935.
 - (h) Bortolozzi, Menenio: Linfogranuloma e reazione biologica di Gordon, *Diag. e tec. di lab.* **6**: 273 (April) 1935.
 - (i) Smith, E. C.: Hodgkin's Disease in Natives of Nigeria, *Lancet* **2**: 874 (Oct. 19) 1935.
 - (j) Rosenberg, D. H., and Bloch, Leon: The Gordon Test for Hodgkin's Disease, *J. A. M. A.* **106**: 1156 (April 4) 1936.
 - (k) Goldstein, J. D.: The Gordon Test for Hodgkin's Disease, *Am. J. M. Sc.* **191**: 775 (June) 1936.
 - (l) Chapman, E. M.: Studies in Hodgkin's Disease, *Ann. Int. Med.* **10**: 742 (Dec.) 1936.
 - (m) Wurm, K.: Zur Frage des Gordontestes bei der Hodgkinschen Lymphogranulomatose, *Verhandl. d. deutsch. Gesellsch. f. inn. Med.* **49**: 228, 1937.
 - (n) Turner, J. C.; Jackson, Henry, Jr., and Parker, Frederic: The Etiological Relation of the Eosinophil to the Gordon Phenomenon in Hodgkin's Disease, *Am. J. M. Sc.* **195**: 27 (Jan.) 1938.
 - (o) Gordon.¹
3. Gordon, M. H.: Aetiology of Lymphadenoma: Sensitized Vaccine of the Elementary Bodies, *Lancet* **2**: 65 (July 11) 1936.
4. Warner, E. C.: The Treatment of Lymphadenoma with a Sensitized Vaccine of the Elementary Bodies, *Lancet* **2**: 417 (Aug. 22) 1936.
5. Kelser, R. A., and King, L. S.: Studies of a Paralysis Syndrome Produced in Rabbits and Guinea Pigs by Extracts of Normal Primate Bone Marrow, *Am. J. Path.* **12**: 317 (May) 1936. Van Rooyen, C. E.: The Interpretation and Significance of Gordon's Test in the Diagnosis of Hodgkin's Disease, *Edinburgh M. J.* **44**: 455, 1937. Chapman.^{2,1} Wurm.^{2m} Turner, Jackson and Parker.²ⁿ
6. Uhlenhuth, P., and Wurm, K.: Zur Frage der Hodgkinschen Lymphogranulomatose, *Klin. Wchnschr.* **15**: 1025 (July 18) 1936. Van Rooyen.^{2b} Chapman.^{2,1}
7. (a) Friedemann, Ulrich, and Elkeles, A.: Studies on the Aetiology of Blood Diseases: A Pathogenic Agent in Normal Human Bone Marrow, *Brit. M. J.* **2**: 1110 (Dec. 16) 1933. (b) Friedemann, Ulrich: The Pathogenic Agent in Normal Human Bone Marrow: Its Nature and Relationship to the Lymphadenoma Agent of Gordon, *ibid.* **1**: 517 (March 24) 1934.

8. Jochmann, G., and Lockemann, G.: Darstellung und Eigenschaften des proteolytischen Leukocytenferments, *Beitr. z. chem. Physiol. u. Path.* **11**: 449, 1908.

9. Gordon, M. H.: Pathology and Treatment of Lymphadenoma, *Brit. M. J.* **1**: 635 (April 7) 1934.

10. MacKenzie, Ian, and Van Rooyen, C. E.: Relationship of Jochmann's and Other Enzymes to the Encephalitogenic Agent in Lymphadenomatous Lymphatic Glands, *Brit. M. J.* **1**: 406 (March 2) 1935.

autopsy were dissected as free as possible from fat and fibrous tissue, and a slice was removed for histologic examination. The remainder was weighed, minced with scissors, ground in a mortar and made into a 10 per cent suspension by the addition of beef infusion broth at a p_H of 7.2. The emulsions in cotton-stoppered test tubes were immediately cultured and then placed in a refrigerator for at least one week and often for two weeks or longer. If the cultures showed growth the emulsions were sterilized with phenol in concentrations as high as 0.5 per cent. When the glandular material was adequate a portion was ground, rapidly dried in a desiccator, transferred to a glass tube, sealed and stored in the refrigerator. After being autolyzed in the refrigerator the original emulsions were centrifuged, and 0.4 cc. of the clear supernatant fluid was injected into the occipital lobe of the brains of rabbits and a similar amount given intravenously through an ear vessel. The animals were observed daily for neurologic manifestations and records kept as to weight and temperature for at least thirty days and often for several months. Occasionally there were immediate paralysis and convulsions after the injection, but the animals so affected were not included in this series unless they appeared entirely normal within a few hours. In positive tests the animals had the rigidity, ataxia and paralysis described by Gordon after an incubation period of from three to fourteen days.

RESULTS

Lymph nodes from fifty patients were tested, some 200 rabbits being used. The nodes were obtained from thirty-seven by biopsy and from thirteen at autopsy. Many of the patients presented some clinical symptoms compatible with the diagnosis of Hodgkin's disease, and all had lymphadenopathy. In thirteen cases the diagnosis of Hodgkin's disease was made by histologic examination, while in the remainder it was based on a variety of pathologic conditions, as listed in the accompanying table, and the latter cases served as controls. The Gordon test was positive in ten of the thirteen cases of Hodgkin's disease (77 per cent) and was negative in three cases. The test was negative in thirty-five of the thirty-seven control cases (95 per cent).

The two control cases in which the Gordon test was positive are worthy of comment:

CASE 1.—A youth aged 18 had mild fever, a palpable spleen, generalized mild lymphadenopathy, clubbed fingers and bilateral bronchiectasis, with copious sputum containing *Streptococcus viridans* (alpha) and a partially hemolytic streptococcus (alpha prime). There were moderate secondary anemia and a leukocyte count of 10,000, with 43 per cent eosinophils. Careful investigation failed to reveal a satisfactory explanation for the eosinophilia. An inguinal and an epitrochlear lymph node were removed for histologic examination and the Gordon test. Both nodes yielded pure cultures of *Streptococcus viridans*. The sections showed chronic hyperplastic lymphadenitis with numerous eosinophils. The Gordon tests were positive. The status of the patient was followed for sixteen months, at the end of which he felt well and had gained considerable weight. The spleen was not palpable, and the superficial lymph nodes were smaller. He raised considerable sputum.

CASE 2.—A man aged 42, who felt perfectly well except for "swellings" on both sides of his neck, was seen at physical examination to be entirely normal except for a chain of hard discrete nodules on both sides of the neck, extending from behind the ears to the supraclavicular regions, and similar nodes in the left axilla and groin. The leukocyte count was 10,300, with 72 per cent polymorphonuclears and 2 per cent eosinophils. Biopsy of a cervical node revealed that a large portion of the lymphoid tissue was replaced by a squamous type of

epithelium with active mitosis. The remaining lymphoid structure was normal except for myriads of eosinophils. A careful clinical and roentgenologic search revealed no primary source for this carcinoma. Gordon tests were positive on the third day in the two rabbits inoculated. Subsequently an axillary node was removed; it was largely replaced by epithelial growth but contained only occasional eosinophils. Unfortunately this biopsy specimen came to me in solution of formaldehyde and a Gordon test could not be performed.

Under roentgen therapy the glands in the various areas receded. The patient was seen at frequent intervals, but it was not until eleven months later that a tumor was demonstrated in the nasopharynx. This region had been examined carefully several times previously. A biopsy of the nasopharynx gave a diagnosis of lympho-epithelioma. This was undoubtedly the primary tumor. A course of supervoltage roentgen therapy caused disappearance of the nasopharyngeal tumor. When the patient was last seen, four months later, there were no evidences of recurrence and he appeared well.

These two positive tests in cases which as far as we could determine were not of Hodgkin's disease caused us to review critically the forty cases in which tests had been made. At that time eight cases of Hodgkin's disease had been studied, and in all but one the Gordon tests had been positive. There were thirty-two controls, and in all except the two cases reported the tests were negative. In an attempt to correlate the histologic structure of the lymph nodes with the response in the rabbits it became evident that the emulsions giving a positive reaction were from nodes rich in eosinophils regardless of the other histologic changes. In order to test the significance of this observation several experiments were performed with suspensions of other human tissues handled in a comparable manner.

Extracts of a cutaneous tumor from a patient with typical mycosis fungoides and from the renal cortex of a patient with subacute glomerular nephritis, both containing numerous eosinophils, gave positive Gordon reactions. Friedemann²⁰ reported that normal human kidney did not elicit this reaction. It may be proposed that this observation indicates the close identity of mycosis fungoides and Hodgkin's disease, but I do not think that it necessarily does.

Rabbit tests were positive after injection of extracts of leukocytic cream separated from the blood of two patients with trichinosis, one with a blood count of 11,000 leukocytes, 31 per cent eosinophils, and the other with a count of 14,200, 54 per cent eosinophils. I have not experimented further with leukocytic creams, but others²¹ have found that any suspension of human leukocytes containing as many as "2,000 eosinophils per cubic millimeter produced a paralysis indistinguishable from that seen in the positive Gordon test, while the numbers of any other type of white blood cell appeared to exert no such influence."

I was curious as to the effects that might be produced by injection of another type of eosinophilic cell, such as that found in the hypophysis. Extracts of the anterior lobe of the hypophysis from a person who had died of an abscess of the lung and empyema and from a patient who had died of bronchopneumonia both gave negative reactions in animals.

During this period nodes from ten more patients with lymphadenopathy were tested, bringing the number of cases to the fifty reported. A study of all the microscopic slides showed remarkable agreement of positive Gordon tests and nodes generously infiltrated with eosinophils. Sections of the nodes from the three patients said by clinicians and pathologists to have Hodgkin's disease but with negative Gordon reactions

revealed exceedingly rare eosinophils. One of these patients died three months after the tests were made and another within a year, and the third is following the usual failing course of Hodgkin's disease.

Eosinophils were remarkably few in number or absent from the sections from the thirty-five control patients giving negative Gordon reactions. Three controls had nodes which histologic examination showed to be tuberculous. When suspensions of these nodes were injected into rabbits, two gave a negative reaction but the third rabbit grew loath to move, showed signs of meningeal irritation, lost weight and died in two and a half months. It did not exhibit the typical sequence of events of a positive Gordon reaction. An autopsy revealed caseous tuberculous lesions in the lungs containing many acid-fast bacilli. There was mild non-specific lymphocytic infiltration of the meninges, but a definitely tuberculous lesion was not demonstrated in the brain. Bacteriologic examination of the original lymph node had shown acid-fast bacilli and *Streptococcus viridans*. The latter had been destroyed by phenol, and it was hoped that the tubercle bacilli were also destroyed, but apparently they were not. Since Manson²⁸ reported positive Gordon tests with nodes from two patients with tuberculosis, I wonder whether his rabbits showed tuberculous lesions of the central nervous system which could possibly have accounted for their neurologic signs or whether there were many eosinophils present in the nodes.

The papers of Gordon and Van Rooyen should be consulted regarding the properties of the pathogenic agent present in emulsions of glands from patients with Hodgkin's disease. I add a few personal observations on the nature of this agent in verification of some of their work.

An autopsy furnished a large amount of typical Hodgkin's lymph glands heavily infiltrated with eosinophils. The patient had received all the roentgen therapy that could be tolerated with safety. Extracts of the lymph glands elicited positive Gordon reactions in three days, with death of the animals in from five to twenty days. One extract was sterilized by long centrifugation, another with phenol and a third by passage through a Seitz filter according to the technic of Van Rooyen.²⁹ All rabbits gave positive reactions on the third day after inoculation. Sixty days later a portion of desiccated gland was made into a 1 to 50 suspension in broth at a p_H of 7.2. One part of the extract was frozen in a test tube in carbon dioxide at -57°C . for ten minutes and then thawed; a second part was exposed in an open vessel to 10,000 roentgens, equivalent to approximately 20 skin doses, and a third part was untreated. All produced positive reactions in rabbits on the third day. It is apparent that roentgen therapy of the living tissue and of the extracted tissue does not inactivate the agent responsible for the reaction in rabbits. Twenty-four months later this desiccated material was still capable of producing a typical Gordon reaction in rabbits when given intracerebrally and intravenously or intracerebrally only. Brains and spinal cords from animals paralyzed by extracts from this patient and from others uniformly failed to produce the Gordon reaction when inoculated into other rabbits either immediately or after extraction.

Kelser and King³ made careful histologic studies of the brains of guinea pigs and rabbits exhibiting the paralytic syndrome after inoculation with extracts of human and monkey bone marrow. They described

reactions occurring locally at the site of injection and also more general widespread effects. The local reaction was similar to that resulting from the introduction of any destructive agent but more severe than that expected from the small amount of material injected. There were central necrosis, hemorrhage and large numbers of Gitter cells, with a peripheral zone of cytologic degeneration, vascular proliferation, perivascular glial infiltration and a mononuclear type of mild meningeal inflammation. The remote reactions were most strikingly seen in the cerebellum, where there was severe and widespread injury to the Purkinje cells. One observes a similar condition in the brains of rabbits exhibiting paralysis after inoculation with extracts of lymph nodes from patients with Hodgkin's disease. Although this phase of the problem will be more carefully detailed at a later date, I reproduce at this time examples of the lesions found. Figure 1 illustrates a field from the inoculation area in the cerebral cortex of a paralyzed rabbit. There are central necrosis, a few Gitter cells, an increase in microglia and a slight

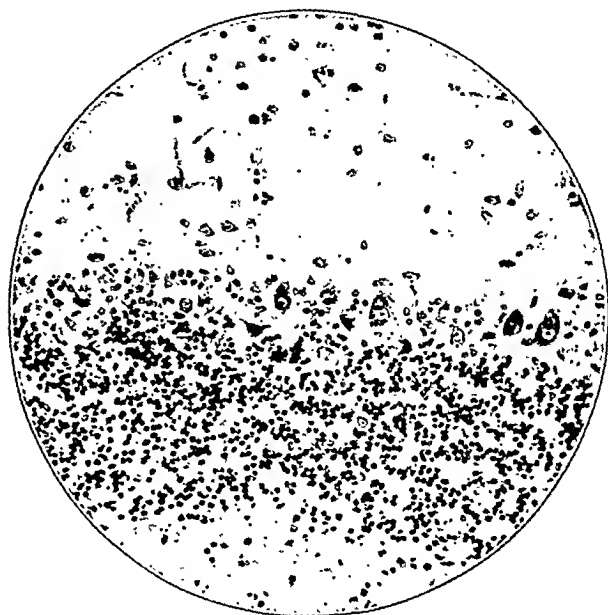


Fig. 2.—The cerebellum of a paralyzed rabbit, showing degenerative changes in the Purkinje cells (slightly reduced from a photomicrograph with a magnification of 160 diameters).

increase in perivascular glial cells. Figure 2 shows part of a folium of the cerebellum of a paralyzed rabbit, with various degenerative changes in the Purkinje cells. These cells are swollen and vacuolated and exhibit neurophagia. Several are pale staining or are mere shadows, while others have completely disappeared. There are fields in the same specimen in which no Purkinje cells can be found.

Kelser and King said that the symptoms of the affected animals are the result of a widespread functional involvement of the nervous system, caused by a chemical or enzymatic agent apparently of leukocytic origin and not by a virus.

COMMENT

The data presented is in confirmation of the conclusions of Turner, Jackson and Parker²⁹ and indicate the close etiologic relation of the eosinophil to the Gordon and Friedemann phenomena. Other writers have published evidence in support of this relation but have attached no significance to their observations.

Wurm^{2m} reported nine cases of clinical and histologic Hodgkin's disease in which the Gordon tests were negative and noted that the sections were singularly free of eosinophils. Van Rooyen⁵ reported a positive Gordon test with material from a boy who clinically had Hodgkin's disease but histologically displayed only marked eosinophilia, with no other features sufficiently characteristic to warrant such a diagnosis. Our compilation of 192 cases of Hodgkin's disease shows that the Gordon test was positive with approxi-

4. Histologic studies have already shown that eosinophils are easily demonstrable in the glands of some 70 per cent of patients with Hodgkin's disease, and it is in the same percentage of cases that the Gordon test is positive. Apparently it is positive only by virtue of these cells.

5. The Gordon test is of no more practical value in the diagnosis of Hodgkin's disease than is the finding of eosinophils in the lymph nodes.

Results with the Gordon Test

Type of Material	Histologic Diagnosis	Number of Cases	Gordon Test	
			Positive	Negative
Lymph nodes	Hodgkin's disease.....	13	10	3
	Lymphadenitis.....	11	1	10
	Leukemia, lymphatic.....	7	0	7
	Leukemia, myeloid.....	2	0	2
	Leukemia, monocytic.....	2	0	2
	Pseudoleukemia.....	1	0	1
	Lymphosarcoma.....	6	0	6
	Tuberculosis.....	3	0	3
	Carcinoma.....	3	1	2
	Retinoblastoma.....	1	0	1
	Endothelioma.....	1	0	1
		50	12	38
Skin:		1	1	0
Kidney:		1	1	0
Leukocytic cream	Trichinosis.....	2	2	0
Hypophysis		2	0	2

mately 70 per cent of the lymph nodes. This is in complete agreement with the critical histologic studies of Pullinger¹¹ on the lymph nodes from thirty-nine patients with Hodgkin's disease, in which eosinophils were found in 71 per cent of the nodes.

It follows that the Gordon test is of little or no value in the practical diagnosis of Hodgkin's disease. It is true that the test is positive with 70 per cent of the lymph nodes from patients with the disease and negative with 98 per cent of other lymph nodes, but this apparently is due only to the eosinophils present and undoubtedly has nothing to do with the disease itself.

The exact nature of the pathogenic agent still remains unknown. It apparently is not a virus or living agent. I favor the theory that it is a chemical or enzymatic agent.⁶ It has been suggested that it may be similar to the Charcot-Leyden crystals, which are looked on as a derivative of the primate eosinophil.^{2m} Future studies may be enlightening as to this agent and as to the eosinophil itself.

SUMMARY

1. In my series the Gordon test was positive in ten of thirteen cases of Hodgkin's disease (77 per cent) and negative in thirty-five of thirty-seven control cases of various lymphadenopathies (95 per cent). These cases being included, the Gordon test has been reported positive in 70 per cent of 192 cases of Hodgkin's disease and negative in 98 per cent of 251 control cases.

2. Histologic sections of the lymph nodes eliciting the positive reactions showed numerous eosinophils, while the nodes associated with the negative reactions contained very few or no eosinophils.

3. Extracts of human tissues and leukocytes which were from patients who definitely did not have Hodgkin's disease but which contained many eosinophils caused reactions in rabbits indistinguishable from those caused by the lymph nodes from patients with typical Hodgkin's disease. This supports the theory that Gordon's agent and Friedemann's agent are identical and are apparently derived from the eosinophil.

11. Pullinger, B. D.: *Rose Research on Lymphadenoma: Histology and Histogenesis*, Bristol, England, John Wright & Sons, Ltd., 1932.

ABSTRACT OF DISCUSSION

DR. F. H. LAMB, Davenport, Iowa: I should like to ask Dr. McNaught what percentage of the cases in which the lymph nodes were tested were from living patients, and how that percentage compares with those from the dead.

DR. JAMES B. McNAUGHT, San Francisco: Lymph nodes from two of the thirteen cases of Hodgkin's disease submitted to the Gordon biologic test were obtained at autopsy. Both gave positive tests. The other eleven specimens were biopsies. Eight of these were positive and three were negative. Other than the simple tests, most of the experimental work was performed on autopsy material, which obviously was available in larger quantities.

Clinical Notes, Suggestions and New Instruments

VINETHENE BURN

SYDNEY S. LYONS, D.D.S., M.D., NEW YORK

Vinethene, since its introduction to clinical anesthesia in 1931, has been the subject of numerous reports. A review of these articles failed to reveal any reference to the possibility of this agent producing a skin burn.



Appearance of burn two days after administration of anesthetic.

Herein is a brief description of a clinical case of a burn on the face which occurred following the administration of vinethene anesthesia.

REPORT OF CASE

A white boy, aged 13, from the psychopathic service, was brought to the dental clinic for extraction. The history and physical examination were irrelevant. The skin of the face was apparently normal. The patient was anesthetized in a dental chair. Vinethene was administered by an open drop

From the Division of Anesthesia, Bellevue Hospital.

technic. This method consisted in cupping a regulation 4 by 4 inch hospital gauze square (40/44 mesh, six thicknesses) over the nose and mouth to form an evaporating surface. Vinethene was then dropped on the gauze from freshly opened original 25 cc. containers until surgical anesthesia was obtained. Less than one minute after induction was begun the gauze was rearranged, permitting the surgeon access to the mouth. Extraction required twenty-one minutes, during which time vinethene was constantly dropped on the gauze held in place by the anesthetist's thumb and finger. After completion of the operating procedure the gauze was removed. A total of 46 cc. of anesthetic agent had been used. Recovery from anesthesia was complete in less than two minutes and the patient soon walked to the ward, accompanied by an attendant. On his arrival he complained of a sore cheek. Some six hours later, a vesicle was noted and examination the following day revealed a superficial lesion lateral to the left ala nasi, which was evidently a burn. The site of the cauterized area corresponded to the position over which the anesthetist placed his thumb to hold the gauze. Its configuration resembled the part of the thumb which had kept contact between the gauze and the face. The burn was treated with boric acid ointment and healing was complete in seven days. A photograph taken on the second day after anesthesia is reproduced.

This case illustrates that vinethene may cauterize the skin as does ether, when it is confined to an area from which it cannot evaporate easily. If pressure is applied to the area it may enhance the possibility of a burn. It is advised that with technics similar to that used in the case reviewed, the skin be protected by applying a bland ointment before administering anesthesia.

Twenty-Sixth Street and First Avenue.

A MICROSCOPIC PRECIPITIN TEST FOR TYPING PNEUMOCOCCI

ISABELLE G. SCHAUB, A.B., AND ROGER D. REID, PH.D., BALTIMORE

The rapid typing of pneumococci is becoming increasingly important with the development of therapeutic serums for the various types. The Neufeld method is admirably suited when the organisms are present in sputum, but difficulties are encountered when typing is attempted from cultures. The macroscopic agglutination of cultures requires the use of pipets and test tubes, and the quantity of serum required represents considerable expense. We have employed a microscopic precipitin technic by which the pneumococci can be typed from cultures quickly and with a very small amount of immune serum. The technic proposed by Brown¹ for grouping the hemolytic streptococci has been adapted for this purpose.

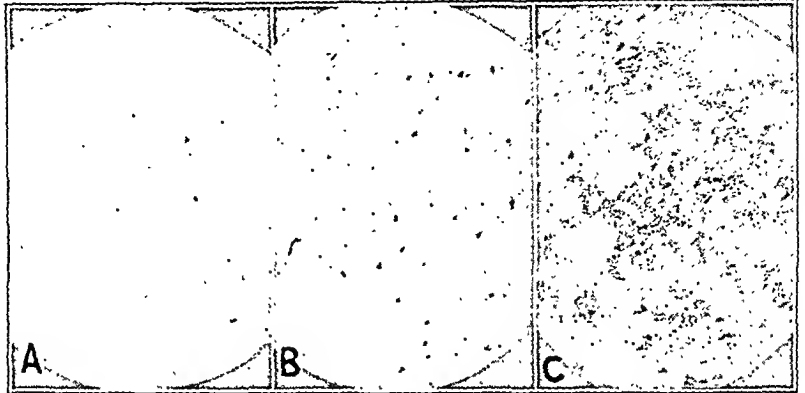
PREPARATION OF THE ANTIGEN

Cultures of pneumococci from blood, spinal fluid or other sources taken during life or at autopsy may be grown in meat infusion broth containing a few drops of serum or ascitic fluid² incubated at 37 C. for from six to eighteen hours. The culture is lysed by the addition of two drops of a 10 per cent aqueous solution of sodium desoxycholate (containing 1:50,000 merthiolate to prevent the growth of molds) per cubic centimeter of

culture.³ In from fifteen to thirty minutes the organisms are dissolved, and tests have shown that the lysate is sterile. The antigen is now ready for use. In some instances an excess of sodium desoxycholate in the presence of serum will cause the culture medium to gel. This may be liquefied by warming slightly without decreasing the efficiency of the test.

PREPARATION OF THE TYPING SERUM

For making this test, horse antipneumococcus serum such as is used for macroscopic agglutination tests, diluted 1:10 in



A, negative precipitin reaction; B, doubtful cross reaction; C, typical positive reaction.

physiologic solution of sodium chloride, is used. Such dilutions have been found satisfactory after refrigeration for as long as six weeks.

Rabbit antipneumococcus serum as prepared for the "quellung" test, diluted 1:1 in salt solution, has been used, but the reaction takes place more slowly, sometimes requiring from one to two hours for marked precipitation to take place. The reaction with the diluted horse serum takes place rapidly, and readings can be made after from fifteen to thirty minutes. By adding 1 per cent aqueous methylene blue to the horse serum the reading of results is facilitated, although the dye is not essential to the test. Dye is already present in the rabbit "quellung" serum.

Attempts were made to place the organisms into groups by means of commercially prepared "quellung" grouping serums or by mixing the typing serums prepared from horses in proportions based on the titer of the species antiserum, but results obtained were not sufficiently uniform to be considered satisfactory.

TECHNIC OF THE TEST

The Petri dish-hanging drop technic described by Brown is used for making the test. A disk of moist filter paper is placed in the lid of the dish. The bottom of the dish is ruled on the bottom surface with a wax or diamond pencil, providing sixteen 12 mm. squares. In the performance of the test two Petri dishes are required for each organism to be typed. In one dish the antigen is set up against each of the fifteen types of antiserum (diluted), the sixteenth square being used for an antigen-salt control. In the second dish the remaining type antisera are set up. It has been found most practicable to add one platinum loopful of the antigen to each of five squares and mix with them an equal amount of the appropriate typing serums, and then to proceed with the next five squares in the same manner. This prevents drying of the loop of antigen before it is possible to add the antiserum, as is likely to happen if the antigen is placed in all fifteen squares before the antisera are added. A 2 mm. loop of platinum rather than one of the platinum substitutes is recommended. The loop should be thoroughly flamed and cooled each time before being introduced into the serum.

READING OF RESULTS

The mixtures of serum and antigen are held from fifteen to thirty minutes and readings are made with the 16 mm. objective of the microscope, the light from the condenser being

3. This method for the preparation of the antigen does not actually introduce an additional step, since solubility in sodium desoxycholate is one of the first tests to be made in the identification of pneumococci. Leifson, Einar: The Use of Sodium Desoxycholate for the Identification of Pneumococci, J. A. M. A. 104: 213 (Jan. 19) 1935.

From the Department of Pathology and Bacteriology, Johns Hopkins University.

The Division of Laboratories and Research, New York State Department of Health, the Bureau of Laboratories, New York City Department of Health, the Bureau of Bacteriology, Maryland State Department of Health, and Sharp and Dohme, Philadelphia, supplied the cultures and antisera for this investigation.

1. Brown, J. H.: A Simplified Method for Grouping Hemolytic Streptococci by the Precipitin Reaction, J. A. M. A. 111: 310 (July 23) 1938.

2. Other mediums such as meat infusion broth with or without blood may be used. A small amount of dextrose may be added to stimulate growth, but in this case it is necessary to adjust the reaction of the medium by the addition of sodium hydroxide until the indicator, bromothymol blue, is bluish green, indicating that the solution is slightly alkaline before the sodium desoxycholate is added. The cultures may also be grown on infusion agar slants containing 10 per cent rabbit blood and the organisms washed off with sterile saline solution and lysed. A satisfactory antigen has also been prepared by using the peritoneal washings from a mouse previously injected with infected material such as sputum.

allowed to pass through the moist filter paper. Gentle rotation of the plates hastens the formation of large clumps of precipitate. The appearance of large clumps of precipitate (C in the illustration) indicates a positive reaction. Negative results are indicated by the absence of such clumping (A). Doubtful or questionable results are seldom encountered but can be eliminated by comparison with the control and a known positive. In using this technic for the first few times it is suggested that known positives and negatives be set up as controls to familiarize the worker with typical reactions.

Infrequently, though occasionally, cross reactions occur. These may be distinguished from typical positive reactions with a little experience. Such a doubtful cross reaction is shown in B. There appears to be no advantage in incubation or refrigeration of the mixtures.

RESULTS

We have made repeated tests on cultures belonging to all the known types of pneumococci, including the Cooper strains. We have also identified and made repeated tests on fifty-five cultures taken from infections and at autopsies. Unknown cultures have been checked by other methods and complete agreement was found in every instance.

With the method described, cultures of pneumococci may be typed in a much shorter time than with the macroscopic test; more reliably, in our opinion, than with the "quellung" test; at a minimum expense for serum and antigen, and with the advantage of working with a sterile antigen.

1833 East Monument Street.

Special Clinical Article

HODGKIN'S DISEASE

SIXTY CASES IN WHICH THERE WERE INTRATHORACIC LESIONS

CLINICAL LECTURE AT SAN FRANCISCO
SESSION

C. B. WRIGHT, M.D.
MINNEAPOLIS

In 1832 Hodgkin reported seven cases of unusual glandular swellings. His description was clinical. In 1865 Samuel Wilks reported thirteen similar cases and named the condition "Hodgkin's disease." In 1926 Herbert Fox¹ reexamined Hodgkin's pathologic specimens and found that of the seven cases three were of Hodgkin's disease, one was of syphilis, one was of tuberculosis and one was probably of lymphatic adenemia. For the next seventy years tuberculosis followed Hodgkin's disease like a shadow. It is difficult to realize today what a common condition glandular tuberculosis was previous to modern food sanitation and the tuberculin testing of cattle. In 1902 Dorothy Reed definitely differentiated Hodgkin's disease from tuberculosis. The two diseases are still occasionally found associated. It is very interesting to compare this condition with that in our series. Four patients had calcified nodes, one had active tuberculosis and Hodgkin's disease in the same mediastinal gland and one had terminal tuberculous pericarditis.

Since 1902 pathologists have added much confusion to the literature with a great variety of names for this disease. Wallhauser² found fifty different names for Hodgkin's disease in 1933.

Read in the Medical Division of the General Scientific Meetings at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 14, 1938.

1. Fox, Herbert: Remarks on Microscopical Preparations Made from Some of the Original Tissue Described by Thomas Hodgkin, 1832, Guy's Hosp. Rep. **86**: 11 (Jan.-April) 1936.

2. Wallhauser, Andrew: Hodgkin's Disease, Arch. Path. **16**: 522-523 (Nov.) 1933.

There is no doubt that biopsy is the most exact method of diagnosis of this disease in the living. This presupposes that the specimen furnishes the pathologist with tissue containing the typical lesions. Therefore it should be taken from a characteristic gland. It should be taken, of course, under the most careful antiseptic conditions, as there is nothing more difficult to deal with than the complication of an infected sinus. When Dorothy Reed cells are present they are pathognomonic. In many slides there are large reticulum cells either singly or in groups, not one of which, however, is a typical Dorothy Reed giant cell. According to Bell³ the increase in the number and size of the reticulum cells is the most constant feature of the disease. Fibrosis is usually present and is usually regarded as indicating an advanced stage, but it may be found early in the disease. In some cases fibrosis is prominent in both large and small lymph nodes; in others it is inconspicuous. The cellular forms of Hodgkin's disease blend with leukemia, and in rare cases one finds a leukemic blood picture with typical Hodgkin's disease in the lymph nodes. There is a similar blending with lymphosarcoma and leukemic reticulo-endotheliosis.

I have reviewed sixty cases of Hodgkin's disease, in all of which, during the period of observation, there were intrathoracic complications; all had been observed long enough so that there was a fairly good clinical history and a physical examination had been made. All the patients had roentgen treatment and were under observation for a considerable period.

Figure 1 shows the first indications of the disease as recorded in the chart from the physical examination or in the history taken from the patient or reported by the referring physician.

The patients did not all have intrathoracic lesions on first examination. Some had them then and the rest acquired them later, while they were under observation; many had complications in other parts of the body. In addition to the more common conditions shown in figure 1, there was a variety of unusual conditions.

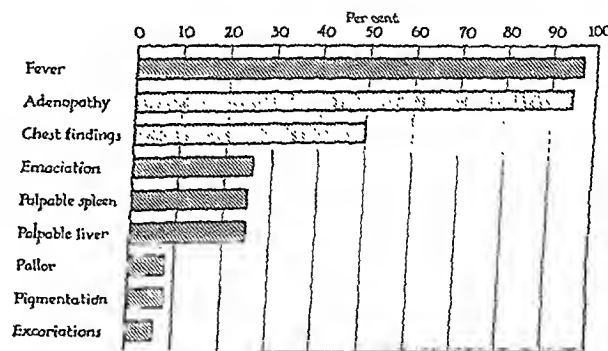


Fig. 1.—First indications of Hodgkin's disease in sixty cases.

In two cases there was jaundice. In one case it was present for about two weeks and then cleared up. In the second case there was a history, on admission, of jaundice coming on about a week after removal of the gallbladder for chronic cholecystitis and cholelithiasis. Glands were later found in the neck which on biopsy proved to be typical of Hodgkin's disease. There were two fatal cases of intestinal perforation due to Hodgkin's disease. There was one case of involvement of the spinal cord with paralysis. There

3. Bell, E. T.: Textbook of Pathology, Philadelphia, Lea & Febiger, 1938.

was one case of extensive involvement of bone and one case of involvement of the skin.

In one case the disease simulated nontropical sprue:

CASE 1.—A woman aged 63 began in 1932 to have diarrhea, generalized weakness and shortness of breath on exertion, and she lost 50 pounds (23 Kg.) in weight. In the fall of 1935 pain in the upper part of the abdomen developed. The liver and spleen became palpable; she had marked secondary anemia, and the white blood cell count was low. The skin was leathery, with a light diffuse pigmentation. No gastrointestinal lesions were found by x-ray study, and a diagnosis of cancer of the liver was suggested. However, with a generous diet and liver the patient gained 20 pounds (9 Kg.) and felt well. Her blood count rose to normal. One year later the diarrhea returned. Three months later vomiting, partial paralysis of the legs, weakness of the hands and slow scanning speech developed. Vibration and the tactile senses were normal. All serologic tests were negative except that for the bacillus of Flexner. The patient had some soreness of the mouth and secondary anemia. No eosinophilia was noted in any of her blood examinations. At times she had a fever, and in her final illness her temperature was as high as 103 F. No superficial glandular enlargements were noted at any time. A clinical diagnosis of nontropical sprue was suggested. The patient died five years after her first symptoms. Postmortem examination showed Hodgkin's disease of the mediastinal nodes, marked Hodgkin's disease of the spleen, tuberculous pericarditis, hyperplasia of the bone marrow, fatty liver with necrosis, chronic benign ulceration of the rectum and pigmentation of the skin.

At no time had she any definite symptoms referable to the chest. The brain and cord were not examined at autopsy.

Fig. 2 (case 3).—Invasion of the left lung and very large mediastinal glands.

any definite symptoms referable to the chest. The brain and cord were not examined at autopsy.

Itching is common in Hodgkin's disease and occurs without lesions other than excoriations:

CASE 2.—A woman aged 41, who complained for eight months of intense itching of the skin, had been treated without improvement. On examination she was found to have enlarged glands in the left supraclavicular region, and biopsy showed typical Hodgkin's disease. X-ray examination showed enlarged glands in the mediastinum. The itching grew less with high voltage roentgen therapy, and the glands disappeared.

Desjardins⁴ expressed the opinion that pruritus and cutaneous lesions could be cured by irradiation over the liver. Roentgen therapy does not always relieve the itching. Kasaback and McAlpin⁵ relieved two of five patients with roentgen treatment over the liver.

Certain clinical and laboratory observations have been used as criteria for the diagnosis of Hodgkin's disease. Discrete, painless and slowly developing enlargement of the peripheral glands is the most common clinical characteristic. Practically all patients have fever.

LABORATORY STUDY

In only eleven of the sixty cases was there eosinophilia. The degree varied from time to time during the

observation. The highest percentage of eosinophils in any case was 24, and in many of the cases no eosinophils were found in the circulating blood. Secondary anemia is a fairly constant sign in the cases of very active involvement. However, in many cases in which the condition seemed severe the blood counts were within normal limits or showed only a slight degree of anemia. The anemia seemed to have no relationship to roentgen treatment; in fact, many of the patients showed improvement in their blood after this procedure. Leukocytosis was a not uncommon manifestation; white blood cell counts as high as 20,000 or 30,000 were recorded. Leukopenia was found not infrequently; the lowest count recorded was 2,300. The degree of leukopenia varied in individual patients. There was no uniformity in any of the blood counts, as they varied with the same patient at different times and with different patients.

In cases in which tissue is not accessible for biopsy a specific test of some kind would be most desirable. Gordon⁶ devised a test which he thought was specific for Hodgkin's disease. It consisted of inoculating broth suspensions of Hodgkin's tissue into the brain of rabbits or guinea pigs, producing a characteristic paralysis. His work was verified by other observers. Friedman showed, however, that the same type of paralysis of the same kind of animals could be produced with extracts of bone marrow, spleen or glands. Turner and Jackson⁷ concluded that this test is positive because of the presence of eosinophils and that it would be negative when eosinophils were absent. In the present series three patients were tested by this method, and the results with two were positive.

Fifty-four patients had superficial glandular enlargements, and biopsies were performed during their period of observation. Five patients had biopsies or were examined post mortem elsewhere. One patient had no



Fig. 3 (case 3).—Results of treatment.

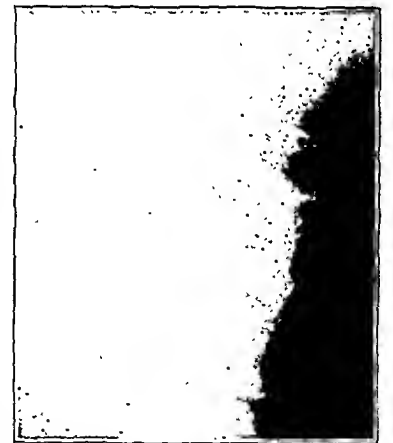


Fig. 4 (case 6).—Extensive involvement of the left ilium.

4. Desjardins, A. U.: Radiotherapy for Hodgkin's Disease and Lymphosarcoma, *J. A. M. A.* 99: 1231-1236 (Oct. 8) 1932.

5. Kasaback, H. H., and McAlpin, Kenneth R.: Mediastinal Hodgkin's Disease, *New York State J. Med.* 38: 171 (Feb. 1) 1938.

6. Gordon, M. H.: Remarks on Hodgkin's Disease, a Pathogenic Agent in the Glands, and Its Application in Diagnosis, *Brit. M. J.* 1: 641-647 (April 15) 1933.

7. Turner, Joseph C., and Jackson, Henry, Jr.: The Etiological Relationship of the Eosinophil to the Gordon Test for Hodgkin's Disease, *J. Clin. Investigation* 16: 657 (July) 1937.

superficial glands showing at any time and therefore no biopsy. In one case the biopsy did not show Hodgkin's disease but autopsy did.

INTRATHORACIC LESIONS

The intrathoracic lesions are of four varieties: (1) enlargement of the mediastinal glands, (2) involvement of the pulmonary parenchyma, (3) involvement of the pleura and (4) combinations of these regional types.

In fifty-seven cases enlarged mediastinal glands were demonstrated by roentgenogram. Twenty-one patients had parenchymal involvement, and eighteen of these had also enlarged mediastinal glands. Three of these patients had parenchymal lesions only. Seventeen patients had pleural effusion; all of these had mediastinal enlargements. Seven had pleural effusion and involvement of the mediastinal glands.

REPORT OF ADDITIONAL CASES

CASE 3.—A man aged 49, who began to have symptoms in 1932 in the form of influenza of the stomach with productive cough, was admitted to the hospital May 8, 1934. It was discovered that he had a tumor which at first was thought to be a bronchiogenic carcinoma. Biopsy of material from a bronchus, however, resulted in a diagnosis of subepithelial fibrosis. Biopsy of an enlarged lymph gland in the axilla showed only hyperplasia. A roentgenogram (fig. 2) showed invasion of the left lung and very large mediastinal glands. The growth responded so remarkably to roentgen treatment (fig. 3) that the diagnosis was changed to lymphosarcoma and later to Hodgkin's disease. The patient was discharged June 2, 1934, and died September 9. No autopsy was performed.

CASE 4.—A girl aged 11, whose first symptoms appeared in October 1930 in the form of swollen glands, began to cough in November 1930. She was admitted to Glen Lake Sanatorium, Oak Terrace, Minn., April 24, 1931, when biopsy resulted in a diagnosis of Hodgkin's disease. The glands enlarged were the left cervical and later the left axillary. Examination of the chest revealed decreased tactile fremitus, dullness and diminished breath sounds over the left portion. The tumor responded very well to roentgen treatment, but the patient died June 24, 1932. No autopsy was performed.



Fig. 5 (case 7).—Extensive tumor.

lateral aspect of the left calf. The chest was clear on physical examination. The patient died November 13, two days after biopsy. No autopsy was performed.

CASE 6.—A man aged 36, who began to have symptoms in September 1933 with pain in the left hip, had experienced marked itching of the skin since 1937. The diagnosis, made by biopsy at the University of Minnesota in January 1938, was Hodgkin's disease. The glands enlarged were the supraclavicular and submaxillary and those in the groins. The thigh was swollen and the left ilium extensively involved (fig. 4). A roentgenogram of the chest showed areas of increased density

in both lung fields, involvement of several ribs and of the left scapula and bilateral involvement of both lungs. The patient died Feb. 6, 1938.

CASE 7.—A girl aged 15 had her first symptom in 1936 in the form of itching, which had been diagnosed elsewhere as scabies. A diagnosis of Hodgkin's disease was made by biopsy at Ancker Hospital, St. Paul, Dec. 15, 1936. The glands enlarged were the cervical, inguinal and epitrochlear. A roentgenogram of the chest (fig. 5) showed enlarged hilar shadows on both sides and mediastinal adenopathy. The itching decreased and there was marked regression of the mediastinal masses with roentgen treatment (fig. 6). The patient was still alive March 10, 1938.



Fig. 6 (case 7).—Almost complete absence of tumor after roentgen treatment.

CASE 8.—A man aged 20, whose first symptoms, in 1924 or 1925, indicated that he had pleurisy with effusion, was well from that time to about November 1928, when he felt weak and had pain in the right axilla. A diagnosis of Hodgkin's disease was made by biopsy at the

University of Minnesota Dec. 27, 1928. The supraclavicular glands were enlarged. Examination of the chest showed increased tactile fremitus, impaired resonance in the upper part of the back on both sides and rales. A roentgenogram of the chest showed a large mass in the right hilus attached to the anterior wall of the chest, posterior to the level of the trachea, and thickening of the pleura on the left side. After treatment the tumor on the right side practically disappeared. Later there was continued improvement on the right side but more evidence of parenchymal involvement at the base of the left lung. The patient died Nov. 8, 1933.

CASE 9.—A youth aged 17 had his first symptoms, consisting of pain in the left shoulder and colds, in May 1934. Swelling in the neck began in August. No biopsy was reported. The patient was admitted to the hospital November 24. The glands enlarged were the left anterior cervical and the right inguinal. Examination of the chest showed dullness over the entire left side. The lower border of the left lung could not be determined. Superficial veins over the chest were dilated. A roentgenogram of the chest showed a large mass, which looked like lymphosarcoma, involving the left side of the mediastinum and another definite area in the right lung. The patient died Dec. 24, 1934; the diagnosis at autopsy was teratoma.

CASE 10.—A man aged 52 had as his first symptom a mass in the upper part of the abdomen and dyspnea, which appeared in September 1935. A tumor was removed in January 1936 and was diagnosed as lymphosarcoma. The patient was admitted to the hospital February 19. One gland was enlarged. A roentgenogram of the chest (fig. 7) showed a suggestion of aneurysm of the descending aorta because of expansible pulsation, metastases in the right pleura and bilateral pleural effusion. When last seen, Oct. 10, 1936, the patient was not responding well to treatment; his condition was worse and the tumor was larger. Autopsy showed a Hodgkin growth completely surrounding the aorta and giving an expansile appearance.

CASE 11.—A man aged 33 had as his first symptoms, in 1928, a sharp pain in the right side of the chest and a temperature between 101 and 102 F. in the afternoon. There was recurrence with cough and effusion in the chest in April 1929. In October 1929 a tumor mass in the mediastinum was found by means of x-ray examination. No biopsy was reported. On admission to the hospital no superficial adenopathy was found. Examination of the chest showed impaired resonance and

increased fremitus over the right side. A roentgenogram showed a small amount of fluid in both sides of the chest and a large mass in the right side of the superior mediastinum, lobular and irregular. The patient was discharged from the hospital Feb. 22, 1930, and died July 10, 1931. Autopsy revealed no Hodgkin's disease, but there were active pulmonary and mediastinal node tuberculosis and amyloid disease.

CASE 12.—A man aged 54, who had as his first symptoms cough and cold, some mucoid sputum, loss of weight and a tendency to tire easily, was admitted to the hospital April 10, 1930. The Wassermann reaction was positive. Fluoroscopic examination of the chest showed a large aneurysm, not pulsating, which extended to the right and left of the mediastinum. A roentgenogram of the chest (fig. 8A) showed an aneurysm of the transverse and descending portions of the arch of the aorta, possibly a double aneurysm, and displacement of the aorta. The patient was last seen Jan. 16, 1931.

CASE 13.—A man aged 21, whose first symptoms were cough, swelling of the face and neck, loss of weight, weakness and shortness of breath, which he had experienced since January 1930, was admitted to the hospital April 9, 1930. Biopsy of the glands in the neck resulted in a report of Hodgkin's disease. The patient had one terrific attack of dyspnea and cyanosis, during which he had to be put in an oxygen tent and tracheotomy was performed. He improved with roentgen therapy. Nodes were present on the right side at the angle of the jaw, there was a mass of glands in the anterior triangle of the neck and veins of the upper part of the chest were dilated. A roentgenogram of the chest (fig. 8B) showed a large lobulated mass extending from the superior mediastinum into both lungs, bilateral pleural effusion and pulmonary abscess. The patient was last heard from Aug. 8, 1930.

THERAPY

Before considering the therapy of Hodgkin's disease I wish to quote from Osler's description published in 1909. He suggested the surgical removal of localized glandular swellings when they are not too large. He also recommended the use of solution of potassium



Fig. 7 (case 10).—Barium sulfate in the esophagus with relation to the growth.

arsenite. At that time x-rays were just beginning to be used and in some cases the condition had responded well. However, he concluded:

There are acute cases in which the enlargements spread rapidly and death follows in three or four months. As a rule, the disease lasts two or three years. Remarkable periods of quiescence may occur in which the glands diminish in size, the fever disappears and the general condition improves. Even a large group of glands

may almost completely disappear or tumor mass on one side of the neck may subside while the inguinal glands are enlarging.

No more is known today about the cause of Hodgkin's disease than Osler knew in 1909. Until the cause is known treatment will be empiric. Surgical intervention at present is seldom used. Solution of potassium arsenite is not mentioned in modern textbooks. The only treatment considered seriously is irradiation.

Reports are appearing from time to time in which the results of roentgen therapy are estimated. Kasaback and McAlpin, in a recent report on a large series of cases, emphasized diet as well as roentgen therapy. Regarding the latter one may conclude:

First, that there is general agreement that high voltage roentgen therapy is not harmful to the patient in doses sufficient to affect this disease.

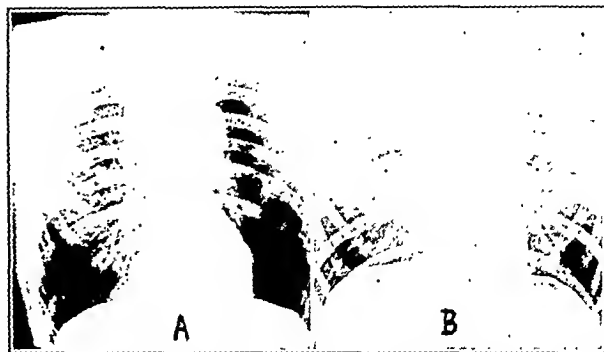


Fig. 8.—A, case 12, syphilis with aneurysm; B, case 13, mediastinal Hodgkin's disease.

Second, that the response to high voltage roentgen therapy of Hodgkin's disease, lymphosarcoma, with which it is most often confused, and to a lesser degree lymphatic aleukemia is as a rule definite and in cases in which the growths are producing pressure on vital organs may be life saving.

Third, that general irradiation of glands and bone is no longer advocated as a prophylactic measure.

Fourth, that the plan now is to treat local manifestations of the disease thoroughly as they arise.

Sensitivity of growths to treatment varies, and the development of resistance to x-rays seems likely. Some patients have this little understood resistance from the beginning; others seem to acquire it after repeated treatment, and the disease rapidly spreads.

The knowledge gathered from tumor clinics will increase, and clinicians should do all they can to assist in therapy. Patients respond well to blood transfusions when anemic, and this procedure also may be life saving. The general edema will often respond remarkably to mercurial diuretics. The diet and general hygienic surroundings should be carefully supervised. One must keep in mind the fact that this disease, which is now generally considered some form of malignant process in the reticulo-endothelial system, may, as some authorities still think, be parasitic in origin.

It is true that the condition in many cases is acute and resists all forms of treatment. The great majority of patients, however, live a considerable length of time, and a few live many years. By means of the available agencies the average period of life can probably be prolonged.

STATISTICAL SUMMARY OF RESULTS OF TREATMENT IN SIXTY CASES

Forty-five of the sixty patients observed were followed until their death. The average duration of life was forty months. Twenty-three of the patients lived over forty months; the average length of life was sixty months. Twenty-one patients lived less than forty months; the average length of life was twenty months. Two patients were lost track of and presumably died, but they are not considered.

For the thirteen patients now living, the average length of the disease is fifty months. Seven of these patients have had the disease seventy-two months. The majority are in fairly good health. Some are working, and others are in a condition of semi-invalidism.

An attempt was made to estimate the length of life after the onset of intrathoracic complications. In some cases there were in addition other complications. In the thirty-nine cases in which this estimate could be made, the average survival period was twenty-three months.

Kasabach and McAlpin found that the average survival period of thirty-eight patients adequately treated was five years and four months. Twenty patients inadequately treated survived three years and three months. In seven cases in which no treatment had been given the survival period was three years and one month.

In our series the shortest period from onset to termination was seven weeks. The patient was a woman aged 40.

The longest period was twenty-six years. In this case the diagnosis of Hodgkin's disease was made by Dr. E. T. Bell in 1910, and several biopsies subsequently confirmed the diagnosis. The patient was treated with roentgen radiation by Dr. Schons from time to time as growths appeared. On three occasions high voltage roentgen therapy apparently saved her life. At autopsy, in 1936, the lesions of Hodgkin's disease were found in the mediastinal and abdominal lymph nodes, liver, spleen and lungs. This case was not included in our statistics.

The following case illustrates the advanced stage in which patients come for treatment:

CASE 14.—A woman aged 51, with a history of easily palpable glands in the right side of the neck and right axilla for three years, when admitted to the Northwestern Hospital had general anasarca, fluid in both pleural cavities and abdomen, involvement of the mediastinal glands, enlargement of the liver and spleen, and large masses in the pelvis, which had led to the diagnosis of possible pelvic carcinoma with metastases. She had marked secondary anemia and a fever. Biopsy showed Hodgkin's disease. She was given salyrgan, blood transfusion and high voltage roentgen therapy over the chest and abdomen. She improved, the edema disappeared, the glands decreased in size, the liver and spleen became smaller and she left the hospital in fairly good health. She died a few weeks later of what appeared to be coronary occlusion. No autopsy was permitted.

Can a patient recover from Hodgkin's disease? The following case is illustrative:

CASE 15.—A man aged 59 had two operations for removal of enlarged glands in his neck. Biopsy by Dr. Bell indicated Hodgkin's disease. The glands recurred the same year and he was treated thoroughly over the neck by high voltage roentgen therapy. He is now 70, has had no subsequent treatment and has had no recurrence after eleven years.

CONCLUSIONS

Hodgkin's is a common disease. The cause is not known. The pathologic changes are well understood, and biopsy is the only sure way of making the diagnosis and should be done early and aseptically. High voltage roentgen therapy is often life saving and if used adequately will probably prolong life. Intrathoracic complications respond well to such therapy. Blood transfusions and mercurial diuretics are at times valuable. The general hygienic surroundings and diet are important.

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Special Article

VITAMIN C

METHODS OF ASSAY AND DIETARY SOURCES

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This article and others recently published or to be published comprise a new series on the present status of our knowledge of the vitamins. They have been prepared under the general auspices of the Council on Pharmacy and Chemistry and the Council on Foods. The opinions expressed are those of the authors and not necessarily the opinions of either council. Reprints are not available but the articles will be published later in book form.—ED.

The isolation, synthesis and development of practical methods of assay have given a great stimulus to the study of vitamin C.¹ More papers have appeared on methods of assay and distribution for vitamin C than for all the other vitamins combined. Therefore, no attempt is made here to present a systematic review of the literature. This has been done amply in the monograph by Sherman and Smith,² the yearly volumes of the *Annual Review of Biochemistry*,³ the bulletin of the United States Department of Agriculture on "Vitamin Content of Foods"⁴ and numerous reviews.⁵ The facts and comments presented in this review may serve to give a general idea of the present state of the subject.

BIO-ASSAY

Chemical methods have rapidly replaced vitamin C determinations by bio-assay for many types of investigations. However, the more specific animal tests continue to be necessary in order to avoid the risk of misinterpretation of the chemical tests.

Guinea pigs kept on certain purified diets fail to gain weight, and the specific pathologic changes of scurvy develop. The degree of protection or cure of the deficiency bears a quantitative relation to the amount of the vitamin administered. This principle forms the basis for biologic methods of vitamin C analyses.

*Preventive Method.*⁶—The technic of Sherman and his associates,² built on the experience of earlier investigators as well as their own studies, has continued to be the most generally used for animal assay purposes. Briefly, the method is as follows: Young guinea pigs are fed ad libitum a basal vitamin C-free diet which theoretically supplies everything necessary for their normal nutrition except vitamin C. Negative control animals are kept on the basal diet only, while other animals are fed graduated amounts of the material to be tested. After from six to ten weeks the degree of protection is estimated by a standard postmortem appraisal of the extent of hemorrhage, the beading and enlargement of the costochondral junctions, the softness of the mandibles, scapulas and ribs, and the looseness of the incisors. An amount of test material just

From Harvard Dental School and the Department of Pathology, Harvard Medical School.

1. Now named ascorbic acid or cevitamic acid.
2. Sherman, H. C., and Smith, S. L.: *The Vitamins*, American Chemical Society Monograph, New York, Chemical Catalog Company, Inc., 1931.

3. (a) Harris, L. J.: *Vitamins*, in *Annual Review of Biochemistry*, Stanford University, Calif., Stanford University Press 1: 357, 1932; 2: 263, 1933; 3: 264, 1934; 4: 347, 1935. (b) von Euler, Hans: *The Water Soluble Vitamins*, *ibid.* 5: 365, 1936. (c) Sherman, Caroline C., and Sherman, H. C.: *The Vitamins*, *ibid.* 6: 346, 1937.

4. Daniel, Esther P., and Munsell, Hazel E.: *Vitamin Content of Foods*, *Miscellaneous Circular 275*, U. S. Department of Agriculture, Bureau of Home Economics, June 1937.

5. King, Fellers.⁶³

6. Sherman and Smith.² Coward.¹⁴ Coward and Kassner.¹⁸

sufficient to afford complete protection from macroscopic scurvy is selected as a unit, and the results of all analyses are expressed in this unit.⁷ With experience and by the use of the survival period, weight and degree of scurvy, one can estimate the degree of protection afforded by the lower test levels, thus bringing into a quantitative rating those animals which are not completely protected. The general uniformity of the test can now be improved by comparing the rate of growth and the intensity of the macroscopic lesions in the test animals with those in a similar group of animals which received graded levels of pure ascorbic acid.⁸

Curative Method.—Harris⁹ and his associates have introduced a recovery method which is very useful. Less material is required and there is considerable saving in time and expense. Guinea pigs are kept on a basal diet as previously described, and after from two to three weeks animals are selected which show symptoms of scurvy and have begun to lose weight evenly. Graduated daily doses of the test material are then fed. After from ten to fourteen days the vitamin C value of the unknown is estimated by comparing the growth response with that obtained by feeding a like series of animals with graded amounts of pure ascorbic acid. Thus, with a continuous supply of guinea pigs acquiring scurvy, a test is completed in about two weeks. Care must be exercised in selecting animals for this test, because those which are "too sick" or which show signs of infection will not respond uniformly.

Tooth Method.—Höjer¹⁰ has proposed a method based on the observation that the degree of scurvy can be estimated by histologic examination of the teeth. A cross section of the root of a normal guinea pig incisor shows a row of long parallel odontoblasts surrounding the pulp and active in the formation of dentin. Höjer has described ten stages in the development of scurvy based on the amount of disorganization of the odontoblasts, the width, irregularity and structure of the dentin and the degree of calcification of the predentin. Key and Elphick¹¹ have described a modification in which, by the same criteria, they distinguish four degrees of scurvy. Using a large series of animals receiving graded doses of ascorbic acid, they plot the average degree of protection against the size of the dose, thus deriving a curve which shows the ratio of protection to dose at any level. When once established, this curve of reference may be used for calculations in successive assays, although it may be revised as additional data accumulate. An example will best show how this curve is used for a determination: A group of healthy growing guinea pigs (from 250 to 300 Gm.) were kept for a few days on a scorbutic diet plus greens. The test was started by withholding the greens. After three days one group of six animals received 0.9 mg. daily of ascorbic acid (International standard). Another group of six animals received 1 cc. of test material (orange juice) daily. Two guinea pigs were kept on the basal

diet only (negative control animals). After fourteen days all the animals were killed and the lower jaws fixed and decalcified in 5 per cent trichloroacetic acid, embedded in celloidin and sectioned just anterior and parallel to the first molar at right angles to the longitudinal axis of the mandible. This method gives a cross section of the incisor root, which runs parallel with the jaw at this point.¹² Sections were stained with hematoxylin and eosin and with connective tissue stains. The degree of protection was scored from 1 to 4 for each tooth and the average obtained for all animals on a like level. The guinea pigs receiving the orange juice showed an average protection of 1.3, while those receiving the ascorbic acid averaged 1.8. On the basis of a curve previously prepared as described by Key,¹³ the ratio of the protection in terms of ascorbic acid was found to be 0.62 divided by 0.90, which equals 0.69. Since, by definition, 1 mg. of ascorbic acid equals 20 international units, the potency of the orange juice equaled 13.8 international units per cubic centimeter. The curve of response is a device for calculating the relative potency of two materials which do not give an identical response.¹⁴ The feeding of a standard with each assay makes possible a correction for differences in sensitivity of different stocks.¹⁵

Comparison of Methods.—The chief source of uncertainty in such quantitative methods lies in the unavoidable variation of individual experimental animals and in the indefinite nature of the end point. Complete protection from scurvy or a definite degree of partial protection are conditions difficult to judge. The answer to the problem of which is the best method of bio-assay for vitamin C depends on the experience of the investigator, equipment available, material to be tested, time available, purpose of the assay and many other factors. In addition to the economy of time, the tooth method or the curative method is most useful if the quantity of test material is limited or subject to change by storage. The specificity of the tooth method and the Sherman method is an important feature lacking from the growth response method of Harris. On the other hand, the two former methods are liable to cause subjective errors in judging the degree of scurvy. The need of histologic experience and special equipment for the tooth method are objections to its general use, while the other methods are adaptable to the usual laboratory equipment. It is my experience¹⁵ and that of others¹⁶ that a longer test period than that recommended by Harris (e.g., four weeks) is necessary to obtain quantitative results comparable with those of other methods.

CHEMICAL METHODS

In general, chemical methods are more rapid and accurate than biologic methods but may lack specificity. However, when available and used with precaution they are of great help in many problems not subject to study by bio-assay.

7. A Sherman unit, or a minimum protective dose, is equivalent to 0.5 to 0.6 mg. of ascorbic acid.

8. International standards for assay purposes are obtained by application to the Protein and Nutrition Division, Bureau of Chemistry and Soils, U. S. Department of Agriculture, or to E. Fullerton Cook, Forty-Third Street and Woodland Avenue, Philadelphia.

9. Harris, L. J., Mills, J. L., and Innes, J. R. M.: The Chemical Identification of Vitamin C, *Lancet* 2: 235 (July 30) 1932. Harris, L. J., and Ray, S. R.: Vitamin C in the Suprarenal Medulla, *Biochem. J.* 27: 2006 (June) 1933.

10. Höjer, J. A.: Method for Determining the Antiscorbutic Value of Foodstuffs by Means of Histologic Examination of the Teeth of Young Guinea Pigs, *Brit. J. Exper. Path.* 7: 356 (Dec.) 1926. Sherman and Smith.

11. Key, Kathleen, M., and Elphick, G. K.: A Quantitative Method for the Determination of Vitamin C, *Biochem. J.* 25: 588 (March) 1931. Key and Morgan.¹²

12. It is important that the section be made at a consistent level of the tooth, otherwise the degenerating odontoblasts which normally occur in the incisal part of the tooth may be confused with the scorbutic process. In a longitudinal section of a guinea pig tooth may be observed dental tissue in all stages of development. In the root the odontoblasts are young, regularly arranged and active in the formation of dentin; as they proceed up the persistently growing tooth, a normal sequence of senility and degeneration occurs. Near the biting end of the tooth the odontoblasts normally have much the same appearance as those which are present in the root in scurvy.

13. Key, Kathleen M., and Morgan, Barbara G. E.: The Determination of the Vitamin C Value of Ascorbic Acid, *Biochem. J.* 27: 1030 (April) 1933. Coward and Kassner.¹⁶

14. Coward, Katherine, H.: The Biological Standardization of Vitamins, *Nutrition Abstr. & Rev.* 4: 24 (April) 1935. Daniel and Munsell.

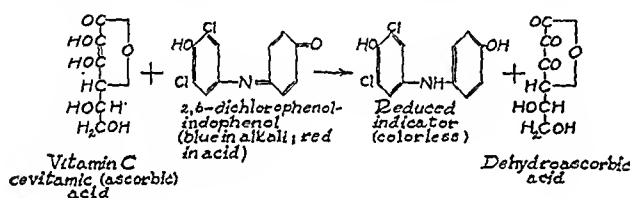
15. Bessey, O. A.: Unpublished data.

16. Coward, Katherine, and Kassner, Elsie W.: The Determination of Vitamin C by Means of Its Influence on the Body Weight of Guinea Pigs, *Biochem. J.* 30: 1719 (Sept.) 1936.

The identification of vitamin C as a substance with striking reducing properties made it apparent that it had been studied previously as an unknown reducing substance in plant and animal tissues.¹⁷ Tillmans¹⁸ in studies of the freshness of natural foodstuffs had pointed out that a reducing substance is present in fresh fruits and vegetables which can be estimated by titration against an indicator, 2,6-dichlorophenolindophenol, and which appears to run parallel with their reported vitamin C content. The establishment of the identity of vitamin C by Waugh and King¹⁹ stimulated experiments by Tillmans and his associates,²⁰ Harris and his associates²¹ and Bessey and King²² which showed the close correlation between the amounts of vitamin C as determined by biological assay and by titration with 2,6-dichlorophenolindophenol in many plant and animal tissues. Additional evidence has supported the view that the titration test when properly used is reasonably specific for vitamin C in natural products.²³

The essential features of the test are an extraction of the material under examination with an acid-precipitating agent to remove certain interfering substances and to stabilize and bring into solution the vitamin C and subsequent titration of the vitamin with a standardized indophenol solution.

The use of 2,6-dichlorophenolindophenol²² to determine vitamin C is based on the fact that the colored



Reduction of indicator solution by vitamin C in acid solution.

indicator solution is quantitatively and rapidly reduced by vitamin C in acid solution to a colorless compound, as represented in the equation.

Indophenol Method.²⁴—The indicator solution is prepared by dissolving the required amount of dry dye in hot water (50 mg. for food and 10 mg. for blood or urine per hundred cubic centimeters). Although the solid dye is stable, the aqueous solution slowly changes even when kept in the refrigerator and for this reason should be restandardized frequently. It is standardized against a carefully prepared solution of ascorbic acid containing 20 ± 0.1 mg. per hundred cubic centimeters of 3 per cent metaphosphoric acid.²⁵ A good commer-

cial ascorbic acid is usually sufficiently pure for this purpose. However, the purity should be checked frequently by titration with iodine.²² One should dilute 5 cc. of the aforementioned solution to 100 cc. with 3 per cent metaphosphoric acid for standardizing the more dilute dye solution. The strength of the reagent is expressed in milligrams of ascorbic acid per cubic centimeter of indophenol solution.

Extracts of plant and animal tissues for vitamin C determinations are best obtained by thoroughly rupturing the cellular structures in metaphosphoric acid. The acid prevents the rapid oxidation of vitamin C due to enzymes²⁶ liberated by the macerated cells or by the presence of traces of certain metals.²⁷ Metaphosphoric acid²⁸ has replaced the use of other acid-extracting reagents because of its marked protective properties and its inertness toward the indicator. Trichloroacetic acid causes fading of the indicator, which may be very rapid with some batches.²⁹ Sulfuric acid reacts with the dye and should never be used.¹⁵ Tungstic acid³⁰ has been used in blood determinations and, although it is a more complete protein precipitant, lacks the protective characteristics of metaphosphoric acid.

An extract of a representative portion of the plant or animal tissue under examination (from 5 to 10 Gm.) is prepared by grinding in a small mortar with sand and fresh 3 per cent metaphosphoric acid until a thin paste is formed. The solids are thrown down in a centrifuge and the clear extract is decanted. Another portion of extracting liquid is used to wash the mortar and is stirred into the solids, which are again centrifuged. The rinsing and washing process is repeated, and the decanted aliquots of the extracts are diluted to 50 cc. Aliquots (10 cc.) of the extracts are titrated with the standard 2,6-dichlorophenolindophenol solution until a faint pink end point is reached. A 10 cc. microburet graduated in 0.01 cc. is convenient.

The indophenol reacts rapidly with vitamin C and should be dropped in at a brisk rate. The end point for most plant tissues is stable for twenty seconds or more, while animal tissues usually fade after from ten to fifteen seconds because of a slow reaction by other substances. Such extracts should be titrated only to an end point at which rapid fading ceases. A correction for the amount of dye required to bring 10 cc. of the extracting acid to the same end point should be applied to all determinations, including the standardizations. This quantity is greater than the usual indicator corrections and should never be neglected. The results are most conveniently expressed in terms of milligrams of ascorbic acid per hundred grams of fresh weight, but in studying vitamin C in tissues which vary considerably in water content, one may get a clearer picture by basing the analysis on dry weight.

Comment.—Since the indophenol method depends on the reduction of the reagent by vitamin C, many substances having a reducing potential lower than the dye are possible sources of interference. However, most such substances found in natural systems react with the

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18. Tillmans, J.; Hirsch, P. and Hirsch, W.: The Reducing Property of Plant Foods and Its Relation to Vitamin C, *Ztschr. f. Untersuch. d. Lebensmitt.* **62**: 1 (Jan.) 1932.

19. Waugh, W. A., and King, C. G.: The Chemical Nature of Vitamin C, *Science* **75**: 357 (April 1) 1932; The Isolation and Identification of Vitamin C, *J. Biol. Chem.* **97**: 325 (April) 1932. Harris, L. J.: Vitamins, in *Annual Review of Biochemistry*, Stanford University, Calif., Stanford University Press **1**: 357, 1932; **2**: 263, 1933.

20. Tillmans, J.; Hirsch, P. and Vanbel, R.: The Reducing Value of Plant Tissues and Its Indication of Vitamin C, *Ztschr. f. Untersuch. d. Lebensmitt.* **65**: 145 (Feb.) 1933.

21. Harris, L. J., and Ray, S. N.: Specificity of Hexuronic (Ascorbic) Acid as Antiscorbutic Factor, *Biochem. J.* **27**: 580 (Feb.) 1933.

22. Bessey, O. A., and King, C. G.: The Distribution of Vitamin C in Plant and Animal Tissues and Its Determination, *J. Biol. Chem.* **103**: 687 (Dec.) 1933.

23. King, C. G.: Vitamin C, Ascorbic Acid, *Physiol. Rev.* **16**: 238 (April) 1936.

24. Harris, L. J.: Vitamins, in *Annual Review of Biochemistry*, Stanford University, Calif., Stanford University Press **3**: 264, 1934. Harris and Ray.²¹ Bessey and King.²² Musulin and King.²⁹

25. Metaphosphoric acid solution is slowly converted to orthophosphoric acid. It should be prepared fresh frequently and should be kept in the refrigerator.

26. Kirtesz, Z. I.; Dearhorn, R. B., and Mack, G. L.: Vitamin C in Vegetables: IV. Ascorbic Acid Oxidase, *J. Biol. Chem.* **116**: 717 (Dec.) 1936. Johnson, S. W., and Zilva, S. S.: The Oxidation of L-Ascorbic Acid by Plant Enzymes, *Biochem. J.* **31**: 438 (March) 1937.

27. Barron, E. S. G.; DeMeio, R. H., and Klemperer, Friedrich: Biological Oxidation: V. Copper and Hemochromagens as Catalyst for the Oxidation of Ascorbic Acid, *J. Biol. Chem.* **113**: 625 (Jan.) 1936.

28. Fujita, Akiji, and Iwatake, Danzo: The Determination of Vitamin C with 2,6-Dichlorophenolindophenol, *Biochem. Ztschr.* **277**: 293, 1935.

29. Musulin, P. R., and King, C. G.: Metaphosphoric Acid in the Extraction and Titration of Vitamin C, *J. Biol. Chem.* **116**: 409 (Nov.) 1936.

30. Taylor, F. H. L.; Chase, D., and Faulkner, J. M.: Ascorbic Acid in Serum and Plasma, *Biochem. J.* **30**: 1119 (July) 1936.

indicator at a perceptibly slower rate than ascorbic acid under the conditions of the titration. This is a requirement for the specificity and accuracy of the method. The end point with plant tissues is stable for some time, but many animal tissue extracts and urines contain sufficient amounts of slow-reducing substances to make the end point less distinct. This is especially true when small quantities of ascorbic acid are being titrated. In such cases the accuracy of the titration depends on the skill of the observer in detecting the point at which rapid reduction is replaced by a slow fading of the indicator. It is true that this feature limits the accuracy of the method, but the precision in most cases is still within the range of biologic variation. The errors are of about the same order as those for blood sugar tests. Unknown reducing materials are reported to interfere with the test in nerve tissue,³¹ eye lens and aqueous humor,³² the liver of some species³³ and tumor tissues.³⁴ Reduction by phenols, tannins, glutathione and many other substances is eliminated by titration in acid solutions below p_H 3. Cysteine, sometimes present in autolyzed tissue, must be estimated separately or removed from the system. Ergothione, thiosulfate, cysteine and other organic sulfur compounds may be removed by a rather impractical mercuric acetate treatment suggested by Emmerie.³⁵ Reductone (glucic acid),³⁶ reductic acid³⁷ and other derivatives formed in hot alkaline sugar solutions reduce the dye in a manner indistinguishable from that of vitamin C. Similar compounds are found in yeast, mold, malt extract and beer.³⁸ These examples illustrate the point that when one is dealing with a type of material not previously checked it is best to establish the validity of the test by other means.

Recent evidence^{38a} suggests that there may exist in certain plant tissues significant quantities of physiologically available combined ascorbic acid which is not extracted by the usual acid extracting reagents and therefore is not included in the titration value. Unless the extracts are carefully prepared and titrated without too much delay, oxidation of vitamin C by liberated enzymes or traces of metals may cause a low titration figure. If the oxidation has proceeded beyond the first step as previously indicated,³⁹ both the chemical and the biologic value will be low. In general, reversibly

oxidized ascorbic acid (dehydroascorbic acid) represents an insignificant portion of the total biologic value of fresh or storage products.

The titration value of some tissue extracts may be increased by preliminary treatment with hydrogen sulfide.³⁵ Some investigators have interpreted this increase as due to reduction of dehydroascorbic acid and have modified the method to include both forms of ascorbic acid. There is some doubt whether it is due to the reduction of dehydroascorbic acid or to the reduction of other substances which are then included in the titration. The uncertainty of the procedure is also increased by the necessity of completely removing the gas because hydrogen sulfide also reduces the indicator. Emmerie and Van Eekelen recommended the use of mercuric acetate to remove cysteine ergothione and of thiosulfate followed by treatment with hydrogen sulfide. The extra manipulation involved, with uncertainty at every step, makes the method at present of doubtful value.

Microtitration with indophenol for special purposes has been described by Birch, Harris and Ray,⁴⁰ Farmer and Abt⁴¹ and Glick.⁴² The last named has applied the Linderstrom technic to microtome-cut sections of glandular tissues with some success.

Other Chemical Methods.—Alternative methods based on the reduction of ferrocyanide,⁴³ phosphotungstic acid,⁴⁴ methylene blue⁴⁵ phosphomolybdic acid⁴⁶ and other color reagents have been proposed. From a theoretical standpoint it would seem that these reagents might be as specific and useful as indophenol, but for one reason or another they have not been widely adopted. In some cases they react too slowly in acid solutions (p_H from 2 to 3 is a necessary condition for specificity). The color changes often vary with time. Many of these reagents react quantitatively with pure ascorbic acid solution but are inhibited or reduced by other materials in urine and tissue extracts. Ascorbic acid in some cases shows side reactions with the reagent, thus interfering with quantitative reduction. A spectroscopic method⁴⁷ in which the intensity of absorption (265 millimicrons) is measured before and after the destruction of the vitamin has been of value in checking the accuracy of the indophenol method. Extracts require special attention in removing irrelevant absorbing materials. Tauber and Kleiner⁴⁸ advocated the determination of reducing capacity before and after the destruction of the vitamin by an oxidase as a means of increasing the specificity of the test. This method is also not entirely specific, because of the nonspecificity of the

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32. Birch, T. W., and Dann, W. J.: Ascorbic Acid in Eye Lens and Aqueous Humor of the Ox, *Biochem. J.* **28**: 638, 1934. von Euler, Hans, and Malmberg, May: Antiscorbutic Action of the Eye Lens and Its Contents of Reductone and Sulphydryl Compounds, *Ztschr. f. physiol. Chem.* **230**: 225, 1934.

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35. Emmerie, Adrianus: Separation of Cysteine from Ascorbic Acid by Mercuric Acetate, *Biochem. J.* **28**: 268, 1934. Emmerie, Adrianus, and Van Eekelen, Marie: The Chemical Determination of Vitamin C with Removal of Interfering Reducing and Colored Substance, *ibid.* **28**: 1153, 1934; Some Critical Remarks on the Determination of Ascorbic Acid, *ibid.* **30**: 25 (Jan.) 1936.

36. Nelson, E. K., and Browne, C. A.: The Properties and Chemical Constitution of Glucic Acid, *J. Am. Chem. Soc.* **51**: 830 (March) 1929. von Euler, Hans, and Martius, Carl: Reductone and Ascorbic Acid, *Ann. d. Chem.* **505**: 73, 1933. King.²³ Nelson and Mottern.³⁹

37. Reichstein, T., and Oppenbauer, R.: Reductic Acid: A Strong Reducing Split Product of Carbohydrates, *Helvet. chim. Acta.* **17**: 390, 1934.

38. Harris, L. J.: Chemical Tests for Vitamin C and the Reducing Substances Present in Urine and Other Tissues, *Nature* **132**: 27 (July) 1933. von Euler.³ Fox and Stone.⁴⁰

38a. Reedman, E. J., and McHenry, E. W.: Combined Ascorbic Acid in Plant Tissues, *Biochem. J.* **32**: 85 (Jan.) 1938.

39. Borsook and his co-workers.³³ King.³⁴

40. Birch, T. W.; Harris, L. J., and Ray, S. N.: A Microchemical Method for Determining the Hexuronic Acid (Vitamin C) Content of Foodstuffs, *Biochem. J.* **27**: 590, 1933.

41. Farmer, C. J., and Abt, A. F.: Determination of Reduced Ascorbic Acid in Small Amounts of Blood, *Proc. Soc. Exper. Biol. & Med.* **34**: 146 (March) 1936.

42. Glick, David, and Biskind, G. R.: The Histochemistry of the Adrenal Gland: I. The Quantitative Distribution of Vitamin C, *J. Biol. Chem.* **110**: 1 (June) 1935; The Histochemistry of the Hypophysis Cerebri: The Quantitative Distribution of Vitamin C, *ibid.* **110**: 583 (Aug.) 1935.

43. Tauber, Henry, and Kleiner, T. S.: A Method for the Quantitative Determination of Ascorbic Acid (Vitamin C), *J. Biol. Chem.* **108**: 563 (Feb.) 1935.

44. Medes, Grace: The Determination of Ascorbic Acid in Urine with Phospho-18-Tungstic Acid, *J. Biochem.* **29**: 2251 (Oct.) 1935.

45. Cal. Imre: Estimation of Ascorbic Acid by Titration, *Nature* **138**: 799 (Nov.) 1936.

46. Bezsonoff, N.: Sur l'identification de la vitamine C, *Bull. Soc. chim. Biol.* **16**: 1107 (July, Aug.) 1934. Bezsonoff, N.; DeLore, A., and Van Wien, H.: L'activité réductrice de la vitamine C et d'autres réducteurs biologiques exprimée en fonction de leur concentration, *ibid.*, p. 1133. Bezsonoff, N., and Van Wien, H.: Sur l'identification et le dosage de la vitamine C dans les milieux biologiques, *ibid.*, p. 1160. von Euler, Hans, and Burstrom, Dagmar: Ascorbic Acid Determinations in Urine by Titration, *Biochem. Ztschr.* **283**: 153, 1936.

47. Robertson, E. B.: Spectroscopic Estimation of Ascorbic Acid, *J. Chem. Industry* **53**: 277 (March) 1934. Chevallier, André, and Choron, Yvonne: Spectrophotometric Method for Estimating Vitamin C in Tissues, *Compt. rend. Soc. de biol.* **125**: 65, 1937.

48. Tauber, Henry, and Kleiner, I. S.: An Enzymic Method for the Estimation of True Vitamin C, *J. Biol. Chem.* **110**: 559 (Aug.) 1935.

enzyme.⁴⁰ Roe⁵⁰ has described a method based on another principle, the color reaction between aniline acetate and furfural, a decomposition product of ascorbic acid.

In general the special features of these procedures are outweighed by features which make them less straightforward and less specific than the indophenol method. A discussion of the weaknesses and merits of all the proposed chemical methods is not within the realm of this paper.

Urine Technic.⁵¹—The excretion of vitamin C in the urine depends primarily on the relative degree of saturation of the tissues and the immediate intake of ascorbic acid. As a state of tissue saturation is approached, the quantity of ascorbic acid excreted in the urine gradually increases until at saturation a marked abrupt elevation occurs. The quantity of ascorbic acid required to induce saturation appears to be a measure of the state of vitamin C nutrition of the patient.⁵²

The analytic procedure for urine is essentially the same as that previously described for tissues. Each specimen of voided urine is measured and a 50 cc. volume containing 10 cc. of 20 per cent metaphosphoric acid is filled to the mark and stoppered. Aliquots should be stored in the refrigerator and titrated within eight to ten hours, during which time relatively little loss occurs. For analysis, the specimen is centrifuged if cloudy, and from 2 to 5 cc., depending on the concentration of ascorbic acid, is diluted to 10 cc. with 3 per cent metaphosphoric acid. The mixture is quickly titrated to a definite pink end point against a standard indophenol solution, a microburet being used. After correction for the titration blank and the added metaphosphoric acid, the total excretion of the specimen is estimated and the twenty-four hour output calculated. The reducing capacity of the urine collected during a preliminary period before the test establishes the excretion level of the patient before treatment with ascorbic acid. This also places the interpretation of the test on a comparative basis, thus correcting for the small constant effect of reducing substances other than ascorbic acid usually present in the urine.⁵³ Heinemann⁵³ has reported a significant interference by thiou sulfate, especially when the diet is high in protein. However, the virtual disappearance of the reducing value in cases of scurvy and extreme deficiency and its restoration at a predicted rate when ascorbic acid is fed contribute strong evidence for the accuracy of the test. Provided manipulations are carried out properly and interpretations of too fine a character are not attempted, the method is of real value.

The estimation of the excretion of ascorbic acid before and after a single dose is also of value in demonstrating the presence of subnutrition of vitamin C. This procedure undoubtedly shows the absence of saturation, but sufficient data have not been collected to allow for an estimation of the degree of deficiency such as is possible by the repeated dose method.

Blood Technic.⁵⁴—The vitamin C level of normal blood plasma as estimated by titration shows a close correlation with the level of intake, thus providing means for evaluating the reserve vitamin C by a single determination for persons in that wide zone between scurvy and saturation (from 0.3 to 1.8 mg. per hundred cubic centimeters). This rapid direct application of the test will undoubtedly replace the less practical urine technic for many purposes.

With slight variations, the procedure now most widely used for blood titrations is as follows: Five or more cubic centimeters of blood is oxalated in a tube which also contains 2 mg. of potassium cyanide, and 2 cc. of plasma is pipetted into 8 cc. of 3 per cent metaphosphoric acid solution. The mixture is stirred, stoppered and centrifuged. A 5 cc. aliquot (equal to 1 cc. of plasma) of the clear centrifugate is immediately titrated, as previously described, with dilute 2,6-dichlorophenolindophenol. After a correction for the blank, which always should be performed parallel with a determination, the ascorbic acid is calculated and expressed as milligrams per hundred cubic centimeters of plasma. All sources of error being taken into consideration, the titration is probably within 0.1 to 0.2 mg. of the true ascorbic acid content of the blood for the range from 0.3 to 1.8 mg. per hundred cubic centimeters. With plasma of lower value, the errors are greater. Cyanide is added to inhibit the slow inactivation of ascorbic acid which occurs in both plasma and filtrate. This is a good precautionary measure against oxidation due to traces of copper and other catalysts, although I have never observed such high rates of destruction in the absence of cyanide as have been reported.⁵⁵ With carefully prepared reagents and water redistilled from glass, the filtrates remain stable for several hours. Metaphosphoric acid is preferred as a deproteinizing agent for reasons previously stated. Plasma is preferred to whole blood for vitamin C determinations because of the greater stability of plasma filtrates.⁵⁶ Substances liberated from red cells by deproteinizing reagents catalyze the inactivation of ascorbic acid even in the presence of cyanide. For this reason plasma which shows evidence of hemolysis is unsuitable for ascorbic acid determinations. Another objection to using whole blood filtrates for vitamin C titration arises from liberation of substances that also reduce the dye. This becomes especially significant when the filtrate is treated with hydrogen sulfide before titration, as recommended by some investigators.

A satisfactory method requiring less blood would be of distinct value in preventing the necessity of venous puncture. Micromethods so far published have not been a solution to this problem. The chief difficulty of titrating such small quantities lies with the inaccuracies of the end point determinations. Mindlin and Butler,⁵⁷ in an unpublished manuscript, propose a method which yields results satisfactory for clinical purposes by the use of from 0.2 to 0.3 cc. of capillary blood. The decrease in concentration of colored indicator produced by the addition of an amount of blood plasma filtrate insufficient to cause complete reduction of the dye is

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50. Roe, J. H.: The Determination of Ascorbic Acid as Furfural and a Comparison of Results Obtained by This Method and by Indophenol Titration, *J. Biol. Chem.* **116**: 609 (Dec.) 1936.

51. Sendroy, Julius, Jr., and Schultz, M. P.: Studies of Ascorbic Acid and Rheumatic Fever: I. Quantitative Index of Ascorbic Acid Utilization in Human Beings and Its Application to the Study of Rheumatic Fever, *J. Clin. Investigation* **15**: 3691 (July) 1936. Harris, L. J., and Ray, S. N.: Diagnosis of Vitamin C Subnutrition by Urine Analysis, *Lancet* **1**: 71 (Jan. 12) 1935. Albassy, M. A.; Harris, L. J.; Ray, S. N., and Marrack, J. B.: Diagnosis of Vitamin C Subnutrition by Urine Analysis, *Lancet* **2**: 1399 (Dec. 21) 1936. von Euler.⁵³ Sherman and Sherman.⁵³

52. Borsook and his co-workers.⁵³ Heinemann.⁵³
53. Heinemann, M.: Dietary Influence on the Amount of Ascorbic Acid and Other Reducing Substances in Urine, *Acta brev. Neerland.* **6**: 67 (Aug.) 1936.

54. Abt, A. F.; Farmer, C. J., and Epstein, I. M.: Normal Cevitamic (Ascorbic Acid) Determinations in Blood Plasma and Their Relationship to Capillary Resistance, *J. Pediat.* **8**: 1 (Jan.) 1936. Ingalls, T. H.: Studies on the Urinary Excretion and Blood Concentration of Ascorbic Acid in Infantile Scurvy, *J. Pediat.* **10**: 577 (May) 1937. Sherman and Sherman.⁵³ Bessey.⁵³ Farmer and Abt.⁵⁴ Pijoon and Klemperer.⁵⁵
55. Pijoon, Michel, and Klemperer, Friedrich: Determination of Blood Ascorbic Acid, *J. Clin. Investigation* **14**: 443 (May) 1937.
56. Borsook and his co-workers.⁵³ Farmer and Abt.⁵⁴
57. Mindlin, R. L., and Butler, A. M.: The Determination of Ascorbic Acid in Plasma: A Macro and Micro Method, *J. Biol. Chem.* **122**: 6732 (Feb.) 1938.

measured by means of a photo-electric colorimeter. This eliminates the subjective reading of the end point. An accurately standardized dye is not needed. Observation of the rate of fading of the color with time permits the detection and study of reducing substances reacting at a slower rate than ascorbic acid.

It is important to emphasize the fact that titrations of blood and many other tissues which are extremely low in ascorbic acid have a limited accuracy even when done with the greatest care. A disregard for this fact is apparent from published investigations. Conclusions based on differences far smaller than the errors of the method used are obviously of doubtful value. Such misinterpretation can be avoided only by a thorough understanding and proper application of the technic.

DIETARY SOURCES

This discussion is concerned with the distribution of vitamin C in food and necessarily lays emphasis on this subject. It should be remembered that adequate nutrition is a problem of supplying many factors in proper proportions and can be met only by use of a variety of foods. Condemnation of a food product because it possesses a low vitamin C value, unless this is a consequence of improper processing or handling, is unjustified. Some foods with many excellent nutritional properties are naturally of low antiscorbutic value.

Ascorbic acid value as far as nutrition is concerned is dependent primarily on two factors: (1) the natural potency of the particular plant or animal tissue and (2) the consequence of aging and processing which occurs before its use as food.

Among the richest sources of vitamin C are oranges, lemons, grapefruit (raw or canned), tangerines, tomatoes (raw or canned) fresh strawberries, green peppers and raw cabbage.⁵⁸

Properly prepared green leafy vegetables have good vitamin C value in spite of the relatively large losses from cooking or canning. In this group may be classed cabbage, spinach, brussels sprouts, kale, broccoli and vegetable greens, such as turnip, beet and dandelion.

Apples, bananas, pineapples (canned), potatoes, green beans and green peas, although containing less antiscorbutic activity, are important sources because of the quantities included in the diet.

The lettuce group, including escarole, have a lower vitamin C content than is generally realized but, since they are usually consumed raw, compare favorably with cooked vegetables. Other important vitamin C-containing foods are kohlrabi, onions, turnips, parsnips and cauliflower.

Dry cereals and legumes of all varieties are devoid of vitamin C, but almost any seed soaked in water for twenty-four hours and kept moist for a few days until it sprouts becomes an effective antiscorbutic substance even when cooked. The British committee on accessory food factors has recommended the use of sprouting seeds as antiscorbutic foods in times of famine.

Cooked muscle meat² is practically free from ascorbic acid, although experience seems to show that if consumed rare or raw in large quantities it prevents scurvy. Liver is greatly superior to muscle in this respect. The distribution of vitamin C in other animal tissues (not important as food) has been discussed in a previous paper of this series.⁵⁹

Butter, eggs and cheese contain no vitamin C. The vitamin C value of commercial pasteurized milk is very small.

*Variety.*⁶⁰—Before the introduction of the chemical method, it was not practical to undertake any comprehensive study of the influence of various factors such as variety, type of soil, season and maturity on the vitamin C potency of fruits and vegetables. Enough information has been obtained now to indicate clearly the need of attention to these points in attempting to obtain food of the highest antiscorbutic value.

Certain varieties of tomatoes⁶¹ contain double the quantity of vitamin C of others grown on the same soil under the same conditions. Canners of tomato juice should give as much attention to this fact as to methods of processing in order to provide the most potent product. Some varieties of apples⁶² are definitely higher in antiscorbutic value than other varieties. Similar consistent differences according to variety have been reported for spinach,⁶³ cabbage,⁶⁴ beans and peas⁶⁵ and probably exist for most fruits and vegetables.

Soil conditions affect the vitamin C content of spinach. Several varieties grown on upland soil were found to average 50 per cent richer than the same varieties grown on muck soil when compared under otherwise similar conditions.⁶⁶ Fall spinach when compared with the same varieties grown in the spring was found to be appreciably higher in ascorbic acid content. It therefore seems likely that crops from year to year may vary in ascorbic acid value because of conditions such as moisture and temperature.

Maturity and Origin.—Tomatoes increase somewhat in vitamin C content as the fruit ripens.⁶⁷ However, mature green tomatoes may have nearly the same value as the red ripe fruit.⁶⁸ The ascorbic acid content of green peppers increases considerably on reddening. A single fruit which is green on one side and red on the other may show a difference of as much as 75 per cent.⁶⁹ A lower vitamin C content in oranges sprayed with lead arsenate has been reported.⁷⁰ Immature Bramley seedling apples are as rich in vitamin C as mature fruit.⁶⁸ Most green leafy and root vegetables contain the greatest concentration of vitamin C during the period of most rapid growth. Sweet corn⁷¹ and green peas⁷² show a maximum vitamin C content during the tender stage, and the content decreases as the seed matures. This is consistent with the lack of vitamin C in nonrespiring mature seeds. Ethylene ripening itself has no effect but tends to encourage early picking and may lead to a slightly lower vitamin C value due to immaturity.⁷³

How and from what most plants and some animals form ascorbic acid is not clear, but the distribution in animal tissues shows it to occur in the greatest concentration in the most actively functioning tissues, in the

60. Daniel and Munsell.⁴ Fellers.⁶³ Tressler, Mack and King.⁷⁰

61. Tripp, Francis; Satterfield, G. H., and Holmes, A. D.: Varietal Differences in the Vitamin C (Ascorbic Acid) Content of Tomatoes, *J. Home Econ.* 29: 258 (April) 1937. MacLinn, Fellers and Buck.⁷¹

62. Smith, G. G., and Fellers, C. R.: Vitamin C Content of Twenty-One Massachusetts Grown Varieties of Apples, *Proc. Am. Soc. Horticultural Sci.* 31: 89, 1934. Batchelder.⁷⁰

63. Tressler, D. K.; Mack, G. L., and King, C. G.: Vitamin C Content of Vegetables: I. Spinach, *Food Research* 1: 3 (Feb.) 1936.

64. Gould, Stella; Tressler, D. K., and King, C. G.: Vitamin C Content of Vegetables: V. Cabbage, *Food Research* 1: 427 (Oct.) 1936.

65. Mack, Tressler and King, footnotes 72 and 73.

66. von Hahn, F. V., and Gorbilg, J.: Influence of Fertilizer on the Vitamin C Content of Spinach, *Ztschr. f. Untersuch. Lebensmitt.* 65: 601 (April-June) 1933. Tressler, Mack and King.⁶³

67. Sherman and Smith.² Tripp, Satterfield and Holmes.⁶¹

68. Fellers, C. R.: The Effect of Processing in Fruit and Vegetables: A Review, *Bull. 338, Massachusetts State College Agricultural Experiment Station, Amherst, December 1936.*

69. Bessey and King.²²

70. Nelson, E. M., and Mottern, H. H.: Effect of Lead Arsenate Spray on the Composition and Vitamin Content of Oranges, *Am. J. Pub. Health* 22: 587 (June) 1932.

71. Dunker, C. F.; Fellers, C. R., and Fitzgerald, G. A.: Stability of Vitamin C in Sweet Corn, *Food Research* 2: 41 (Jan.) 1937.

72. Mack, G. L.; Tressler, D. K., and King, C. G.: Vitamin C Content of Vegetables: II. Peas, *Food Research* 1: 231 (May) 1936.

73. Chace, E. M.: Health Problems Connected with Ethylene Treatment of Fruit, *Am. J. Pub. Health* 24: 1152 (Nov.) 1934.

58. Sherman and Smith.² Daniel and Munsell.⁴ Fellers.⁶³ Sherman.⁵³

59. King, C. G.: Vitamin C Chemistry, *J. A. M. A.*, to be published.

adrenal cortex, corpus luteum, thyroid, pituitary body and liver. This distribution proves to be true also in leaves and growing shoots and suggests a fundamental concern with respiratory processes. However, many rapidly growing fruits are low in ascorbic acid, and the respiratory activity of lemons, oranges and tomatoes does not seem to be unusually high, although these are among the richest sources of ascorbic acid. Eggs and seeds are devoid of vitamin C, but the vitamin forms immediately from unknown constituents when a chick embryo develops or the seed sprouts.

Storage.⁶⁸—Time, temperature, care in handling and type of product are important factors in the problem of the stability of vitamin C during storage. Spinach which has stood for a few days at room temperature and has become wilted loses about one half of its ascorbic acid, while the same spinach kept at 37 or 38 F. for the same period retains its original value.⁷⁴ This is true in general of green leafy vegetables of this type. Cabbage stored at room temperature loses about 25 per cent of its vitamin C in a month, while at 45 or 50 F. the loss is only 10 per cent.⁶⁴ Green beans and peas, like spinach, rapidly lose their ascorbic acid at room temperature but keep well by refrigeration.⁷⁵ Sweet corn in the husk retains its vitamin C well for two or three days, after which time a slow loss occurs.⁶⁸ Green peppers remain rich sources of ascorbic acid for several weeks if they do not become bruised or wilted.¹⁵ Loss in apples after three months at 45 F. approximates 15 per cent, at six months 25 per cent and at one year 50 per cent.⁷⁶ Lemons and oranges stored at 45 or 50 F. for ten months show losses of from 10 to 30 per cent; no detectable loss occurs in two months.¹⁵ Storage of ripe tomatoes at ordinary temperature for a month causes little change in the vitamin C content provided the fruit remains firm and free from bruises and rot.⁷⁷ Potatoes very slowly lose their vitamin C under market conditions; about a 50 per cent loss occurs in one year.²² With some varieties, little loss is observed after from three to six months' storage.⁷⁸ Vitamin C in rutabagas, carrots, turnips and sweet potatoes is slowly lost over a period of several months.⁶⁸

These facts demonstrate the great variation in "storage stability" of vitamin C and indicate the advantage of cold storage as compared with ordinary storage.

Freezing.—Preservation of fruits and vegetables by quick freezing has become an important commercial method.⁷⁹ Studies on the stability of vitamin C during freezing and storage in general have shown slight destruction, but often incidental processing operations such as shelling, washing and blanching lead to significant losses. Asparagus, apples, potatoes, strawberries, blackberries and orange juice are unaffected by freezing, while some losses are reported in preparatory operation with peas, beans and spinach. Freezing results in a certain amount of cellular disorganization, with liberation of enzymes from some types of plant tissues. Unless these products are properly blanched (to destroy enzymes) before freezing, considerable losses may occur during storage and thawing. Slow-thawing vegetables

rapidly lost their vitamin C. Losses of from 80 to 90 per cent may occur in beans, peas or spinach in a few hours. Frozen foods should not be defrosted until ready to cook or serve raw. Losses are reduced to a minimum by cooking without preliminary defrosting.

Processing.—For several reasons, effort should be made to conserve the vitamin C values of the general food supply rather than to depend on the use of foods of special antiscorbutic properties. A larger percentage of the people than is generally realized, because of economic conditions, lack of knowledge or poor food habits, do not include citrus fruits, tomatoes or other richly antiscorbutic foods in their diet. These people necessarily depend on the general food supply for their source of this essential. Also the loss of important food qualities, such as flavor and the content of other vitamins, usually parallels the destruction of vitamin C. In fact, the preservation of ascorbic acid may well be used as a general index to the care with which certain foods have been processed.

The preservation of vitamin C between harvesting and consumption is essentially a problem of combating oxidation, a process dependent on time and the kind and state of the tissue and influenced by temperature, access to air and presence of metals and enzymes. The destruction of vitamin C when tomato juice is heated can be reduced two thirds by rendering the conditions anaerobic.⁸⁰ Spinach and cabbage cooked by methods excluding air are from 50 to 100 per cent richer in vitamin C than when prepared by open kettle cooking.⁸¹ The water in which vegetables are cooked may contain sufficient oxygen to become an important factor of destruction.⁸² This fact has led to the practice of starting vegetables in hot water.

Crushing or bruising of many vegetables such as spinach, cabbage, turnips and rutabagas causes the liberation of enzymes (oxidases) which in the presence of air catalyze the oxidation of ascorbic acid.²⁰ This is a rapid reaction and may lead to complete inactivation of the injured tissue in a few minutes. Starting the cooking in hot water quickly inactivates these enzymes. Shredded carrots, cabbage and other roots and leafy tissues rapidly decrease in vitamin C content and should therefore be prepared fresh before serving.

Vitamin C is more stable in an acid medium than in a neutral or slightly alkaline medium.⁸³ The addition of soda to cooking vegetables may produce a better color but will lead to increased loss of vitamin C. The vitamin C in tomato juice is naturally stable but becomes rapidly inactivated when neutralized or made alkaline with soda. In general, vitamin C is less subject to oxidation in those fruits and vegetables which are acid.

There is perhaps no single factor which accelerates the destruction of vitamin C so much as copper salts. The presence of air and the merest traces of copper lead to complete inactivation often in a few minutes. Contact with bare copper or utensils made of metal containing copper must be avoided. Quantities of copper so small as to be undetectable by the usual chemical methods will lead to immediate and complete destruction of the ascorbic acid in raw milk or cooking vegetables.⁸⁴ The insidious nature of this factor makes it

74. Tressler, Mack and King, footnotes 63 and 75.

75. Tressler, D. K.; Mack, G. I., and King, C. G.: Factors Influencing the Vitamin C Content of Vegetables, *Am. J. Pub. Health* 26: 905 (Sept.) 1936.

76. Batchelder, Esther L.: Vitamin C in Apples, *J. Nutrition* 7: 647 (June) 1934.

77. MacLinn, W. A.; Fellers, C. R., and Buck, R. E.: Tomato Variety and Strain Differences in Ascorbic Acid (Vitamin C) Contents, *Am. Soc. Horticultural Sc.* 34: 543, 1937.

78. Fellers.⁶⁵ Wood.⁸⁵

79. Nelson, E. M., and Mottern, H. H.: Vitamin C Content of Frozen Orange Juice, *J. Indust. & Engin. Chem.* 25: 216 (Feb.) 1933. Daniel and Munsell.⁴ Fellers.⁶⁵ Tressler, Mack and King.¹⁵

80. Kohlman, Eddy and others.⁸² Sherman.⁸³

81. Sherman and Smith.² Bessey.¹⁵

82. Kohlman, E. F.; Eddy, W. H., and Gurin, C. Z.: Vitamins in Canned Foods: XI. A Canned Food Diet, *J. Indust. & Engin. Chem.* 25: 1064 (Sept.) 1933; Canning Tomato Juice without Vitamin C Loss, *ibid.* 25: 682 (June) 1933.

83. Sherman, H. C.: *Chemistry of Food and Nutrition*, ed. 5, New York, Macmillan Company, 1937.

84. Whitnah, C. H.; Riddell, W. H., and Caulfield, W. J.: The Influence of Storage, Pasteurization, and Contamination with Metals on the Stability of Vitamin C in Milk, *J. Dairy Sc.* 19: 373, 1936. Bessey.¹⁵

very difficult to control, for, in addition to contamination by contact and from the water supply, many foods naturally contain enough copper to be active.

Drying⁸⁵ in itself is not detrimental to vitamin C, but for most foods it is almost impossible to prevent oxidation due to other factors sufficiently to prepare dehydrated products of important and lasting antiscorbutic values. Dehydrated foods have repeatedly failed in this respect when used in times of war. Many experiments have been reported showing that certain of the more acid fruits may be prepared so as to conserve a reasonable degree of their vitamin C activity, but commercial products cannot as yet be considered dependable in this respect.

agreement with the previous emphasis on the unfavorable "influence" of contact with copper utensils, access to air, prolonged heating and alkalinity. Modern commercial canning, with careful plant control, can prepare products with a minimum loss of vitamin C which are comparable to carefully cooked fresh food. However, no rule can cover all cases, for there are badly controlled canneries as well as bad cooks. The variations in processing are so great that the products from each process and perhaps each batch would have to be tested before one could be sure of the vitamin C value. Boiling of cabbage in an open kettle or cooking in a pressure cooker leads to almost complete destruction, while starting the cabbage in boiling water and testing both the

The Vitamin C Content of Various Foods per Hundred Grams *

Food	Mg. of Ascorbic Acid	International Units	Food	Mg. of Ascorbic Acid	International Units	Food	Mg. of Ascorbic Acid	International Units
Apples			Cranberries.....	10	200	Papaya.....	40	800
Delicious.....	2.5	50	Cucumbers.....	2	40	Parsley.....	175	3,500
Jonathan.....	2.5	50	Currants, black.....	100	2,000	Parsnips.....	5	100
McIntosh.....	2	40	Currants, red.....	15	300	Peas, green.....	15	300
Winesap.....	5	100	Dandelion greens.....	40	800	Peas, canned.....	5	100
Golden delicious.....	4	80	Dates, cured.....	0	0	Peaches, fresh.....	7	140
Yellow Newton.....	5	100	Egg plant.....	5	100	Peaches, dried.....	25	500
Dried.....	0	0	Eggs.....	0	0	Pears, fresh.....	3	60
Juice.....	See type of apple		Endive.....	10	200	Pear juice, canned.....	Trace	Trace
Apricots, fresh.....	1	20	Escarole.....	7	140	Peppers, green.....	180	3,600
Apricots, dried.....	5	100	Figs, fresh.....	2	40	Peppers, red, ripe.....	230	4,600
	20	400	Figs, dried.....	0	0	Pineapple, fresh.....	25	500
	6	100	Fish, fresh cooked.....	Trace	Trace	Pineapple, canned.....	10	200
Asparagus			Fruit juice.....	See fruit		Plums.....	2	40
Green.....	10	200	Gooseberries.....	25	500	Potatoes, new.....	15	300
	4	80	Grain, dried, all varieties..	0	0	Potatoes, old.....	7	140
	10	200	Grass, fresh, green.....	60	1,200	Prunes.....	2	40
Dried.....	0	0	Grape juice.....	Trace	Trace	Prunes, dried.....	0	0
Beef muscle, cooked.....	Trace	Trace	Grapefruit juice, fresh.....	40	800	Pumpkins.....	5	100
Beer.....	0	0	Grapefruit juice, canned.....	30	600	Quince.....	5	100
Beets.....	5	100	Horseradish.....	100	2,000	Radishes.....	12	240
Beet leaves.....	35	700	Jelly.....	0	0	Raisins.....	0	0
Blackberries, fresh.....	3	60	Kale.....	50	1,000		15	300
Blackberries, frozen.....	3	60	Kohlrabi.....	70	1,400		15	300
Blackberries, low bush.....	4	80	Leek.....	15	300		20	400
Blueberries, high bush.....	10	200	Lemon juice					
Broccoli.....	50	1,000	Fresh.....	60	1,200	varieties).....	0	0
Brussels sprouts.....	50	1,000	Cold storage.....	40	800	Spinach, fresh.....	60	1,200
Butter.....	0	0	Canned.....	50	1,000	Spinach, canned.....	5 to 10	100 to 200
Cabbage, young, green.....	40	800	Lettuce, green leaf.....	10	200	Sauerkraut juice.....	0 to 5	0 to 100
Cabbage, old.....	20	400	Lettuce, head.....	5	100	Squash.....	3	60
Caiflower.....	7	140	Lime juice, fresh.....	30	600	Strawberries.....	25	500
Carrots.....	3	60	Liver, beef, cooked.....	10	200	Sweet potatoes.....	8	160
Cauliflower.....	30	600	Malt.....	0	0	Swede.....	See rutabaga	
Celery stalk.....	5	100	Milk			Tangerines.....	30	600
Chicory.....	10	200	Min an.....	6	120	Tomatoes		
	5	100	Cow's, raw, fresh.....	2	40	Green.....	20	400
	20	400	Cow's, pasteurized.....	0 to 1	0 to 20	Vioe ripe.....	30	600
	0	0	Cow's, dried.....	5	100	Artificial ripe.....	25	500
Cherries, sweet.....	8	160	Mustard leaves.....	60	1,200	Tomato juice, fresh.....	30	600
Cider, fresh.....	See apples		Nuts, all kinds.....	0	0	Tomato juice, canned.....	25	500
Chicken meat, cooked.....	Trace		Okra.....	10	200	Turnips.....	30	600
Cod liver oil.....	0	0	Onion.....	10	200	Turnip greens.....	60	1,200
Collard.....	60	1,200	Orange juice, fresh.....	50	1,000	Vegetable juices canned.....	0 to 5	0 to 100
Corn			Orange juice, canned.....	45	900	Watercress.....	50	1,000
Sweet.....	10	200	Orange syrup.....	0	0	Watermelon.....	5	100
Canned.....	6	120				Yeast.....	0	0
Dried.....	0	0						

* Unless otherwise indicated, these values are on fresh foods.

Pickling, salting, curing or fermenting usually results in complete loss of vitamin C. Fresh cucumbers contain from 5 to 8 mg. per hundred grams; salt pickles contain none. Fermented cider and other fruit juices are free from vitamin C. Sauerkraut and sauerkraut juice are unreliable antiscorbutic foods.⁸⁶ Commercial orange drinks which do not contain freshly prepared orange juice are practically free from ascorbic acid.⁸⁷ Vegetable juices rapidly lose their vitamin C because of active enzymes and a high p_H and therefore are usually poor antiscorbutic foods.

It is difficult to make general statements concerning the loss of vitamin C during such a variable process as cooking⁸⁸ or canning. Recent work is in essential

cooking water and the cabbage produce about 25 per cent destruction and 25 per cent loss in the water.⁶¹ Similar studies on spinach, turnip greens and green peas and beans lead to approximately the same conclusions. Commercial canning destroys from 50 to 85 per cent of the vitamin C in peas, lima beans, spinach and asparagus. Home-canned tomato juice is as satisfactory as commercial canned juice, and both are good antiscorbutic substances.² Vitamin C is stabilized by acid and therefore suffers less destruction during cooking in acid fruits and vegetables. Canned grapefruit and orange juice are about 70 to 90 per cent as potent as the fresh juice and, like most canned products, remain stable while canned but slowly lose their vitamin C when left open to the air.⁸⁷ Baked and boiled potatoes are reported to show only small losses unless overcooked.⁸⁹ Fruit jel-

85. Fellers.⁶³ Sherman.⁵³
86. Sherman and Smith.² Fellers.⁶³
87. Bessey.¹³ Fellers.⁶³
88. Sherman and Smith.² Gould, Tressler and King.⁶¹ Fellers.⁶³
Sherman.⁵³

89. Wood, E.: The Vitamin C Content of the Russel Burbank Potato of Idaho, Bull. 219, University of Idaho Agricultural Experiment Station, June 1935. Fellers.⁶³

lies and jams are usually low in vitamin C. Warmed over foods are practically free from ascorbic acid. Canned or cooked apricots, peaches, plums and cherries are practically free from vitamin C. Freshly prepared apple sauce or apple pies retain from 20 to 30 per cent of the original vitamin C value of the apple.⁹⁰

The use of canned sieved vegetables and fruit for children has increased at a rapid rate in the last few years.⁹⁰ In spite of the most careful methods of processing, partial destruction of vitamin C is unavoidable. A great deal of variation in this occurs, depending on the type of food, freshness and method of processing, but in general it has been shown that the loss of vitamin C is slightly greater for purées than for the corresponding canned whole vegetables. As a rule these products cannot be classed as potent antiscorbutic foods, although they may contribute materially to the diet because of the quantity consumed.

Milk is the most nearly perfect and the least dispensable food. Nevertheless, the vitamin C content of commercial milk, raw or pasteurized, is not dependable and should never be relied on to supply the requirements. The use of the titration method has led to a better understanding of those factors which may influence the vitamin C content of milk, such as aging, pasteurization and handling. Judging from a large number of determinations, both biologic and chemical, one may expect from 2 to 2.5 mg. per hundred cubic centimeters of ascorbic acid in fresh raw milk.⁹¹ Even when the milk is cold this value slowly decreases, until a loss of from 20 to 30 per cent may occur in twenty-four hours. Sunlight or traces of copper accelerate this change.⁹² Pasteurization by the widely used holding method, unless unusual precautions are observed, results in a loss of from 30 to 60 per cent. However, pasteurization by the short time high temperature process with absence of copper leads to slight inactivation.⁹³ Loss of vitamin C activity due to pasteurization, aging, reheating and diluting, such as usually occurs in preparing a formula for babies, results in a formula of very low antiscorbutic value.¹⁵

Although Hess⁹⁴ found that a pint of milk a day prevented infantile scurvy, the commercial milk of today, which contains from 0.3 to 1 mg. per hundred cubic centimeters, is a rather poor source of vitamin C. The 5 mg. of ascorbic acid represented by a pint of average commercial milk is far below that recommended for optimum nutrition. This fact has led to the general use of orange juice, tomato juice or potent antiscorbutic substances as a supplement to the infant diet. A breast-fed infant of a normally nourished mother receives from 20 to 40 mg. of ascorbic acid daily from the day of birth, because human milk is from four to six times richer in vitamin C than cow's or goat's milk.⁹⁵ The implication is strong that vitamin C should be a constituent of the infant's diet at a very early age.

The ascorbic acid value of canned or dried milk? depends primarily on the method by which the milk is prepared or handled. Commercially evaporated milk which has been sterilized at a high temperature is almost free from vitamin C, while sweetened condensed milk which has been evaporated in vacuum at lower temperatures retains a proportion of vitamin C comparable to that of pasteurized milk. Several investigators have reported good conservation in dried milk.⁹⁶ However, most commercial preparations are practically free from vitamin C.¹⁵

The vitamin C concentrations of individual foods are summarized in the accompanying table. Most of the analyses reported were on fresh material. It is difficult to estimate values for cooked or processed food because of the lack of uniformity of methods and treatment. Lower vitamin C values than those given must be expected because of immaturity, lack of freshness, poor preservation, long storage or results of processing. The figures given are estimates derived after consideration of the available data,⁹⁶ including the results of many unpublished analyses from my own laboratory, and represent my judgment of the expected value of the raw edible portions under good market conditions. The value when the food is ready for serving will depend on the method of preparation. A recent United States Department of Agriculture bulletin⁴ contains fuller details of the vitamin C contents of foods and also references to the literature.

Council on Physical Therapy.

THE COUNCIL ON PHYSICAL THERAPY HAS AUTHORIZED PUBLICATION OF THE FOLLOWING ARTICLE. HOWARD A. CARTER, Secretary.

AIR FILTRATION

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By air filtration is implied the removal of impurities, usually in the form of dust, from the air. The benefits derived from such treatment of the air are of great importance in industry as well as in the control of many respiratory diseases.

It can be stated that no air is free from dust. Dust comes from almost every process in which there is disintegration of materials and is thrown into the air by any method that will disturb the dust. Once the particles are in the air, they will remain suspended for varying periods of time, from a few seconds to years, depending on their size and density. Particles of dust differ in size from those which can be seen only by an ultramicroscope to those which are easily discerned by the naked eye, particles 10 microns in size or larger. However, the particles of most concern in their effect on the human body are those from 0.5 to 100 microns in size.

The concentration of dust particles in the air varies greatly, depending on the conditions operative in the locality where samples are taken. In country air which is comparatively clean, especially after a rain, the particles may be as low as a few thousand per cubic foot

90. Fellers, C. A.: Vitamin Content of Important Food in the Child's Diet, *Am. J. Pub. Health* 25:1340 (Dec.) 1935. Hanning, Flora: Comparison of the Biological and Chemical Method for the Determination of Vitamin C in Canned Strained Vegetables and a Study of Its Variation from Year to Year, *J. Nutrition* 12:405 (Oct.) 1936.

91. Rasmussen, Russel, and Gnerant, N. B.: The Effect of Breed Characteristics and Stage of Lactation on the Vitamin C (Ascorbic Acid) Content of Cow's Milk, *J. Nutrition* 11:425 (May) 1936. Riddell, W. H.; Whitnah, C. H.; Hughes, J. S., and Leimhardt, H. F.: Influence of the Ration on the Vitamin C Content of Milk, *J. Nutrition* 11:47 (Jan.) 1936. King and Waugh.⁹³

92. Kon, S. K., and Watson, M. B.: The Effect of Light on the Vitamin C of Milk, *Biochem. J.* 30:2273 (Dec.) 1936. King.⁹³

93. King, C. G., and Waugh, W. A.: Effect of Pasteurization on the Vitamin C Content of Milk, *J. Dairy Sci.* 17:489, 1934. Schwartz, E. W.; Murphy, F. J., and Hann, R. M.: Studies on the Destruction of Vitamin C in the Boiling of Milk, *J. Nutrition* 2:325 (March) 1930.

94. Hess cited by Sherman.⁹⁵
95. Selles, Ina, and King, C. G.: The Vitamin C Content of Human Milk and Its Variation with Diet, *J. Nutrition* 11:599 (June) 1936.

96. Daniel and Munsell.⁴ Fellers.⁹⁰ Lack of space prevents reference to many of the papers considered.
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of air, whereas city air will contain from five hundred thousand to two or three million particles per cubic foot. In heavy industrial centers the contamination has run as high as twenty million particles per cubic foot. Recent studies bear out previous observations of air pollution in both urban and rural areas.¹ In many industries the dust level is tremendous.

The normal concentration of permanent dust in the air is not of much concern, as it actually serves a useful purpose in reflecting light and forming nuclei for rain drops. There are, however, great objections to certain kinds of dust and to their heavy concentrations. In addition to the economic loss due to dust, the effect either direct or indirect on health is often of vital importance.² If the concentration is of sufficient magnitude, ultraviolet rays may be shut off.³ Dust as nuclei for fine droplets of water may form fog in heavy industrial areas.

The direct effect of dusts on health depends to a large extent on their chemical composition and the size of the particles. In many industries dusts and fumes are liberated in sufficient quantities to be injurious to the health of the workers. Many such dusts are direct poisons, as arsenic, lead, mercury, manganese and cadmium. Lead poisoning is a classic example of a disease due to such an occupational hazard. Inhalation of other solid and gaseous ingredients of city air, such as carbon and sulfur fumes, irritates the mucous membranes of the nose, throat and lungs, producing discomfort, and in some instances it may cause injury to health.⁴ In addition, the inhalation over long periods of fine inorganic dusts, such as silicates, iron, carbon and asbestos, leads to the fibroid condition of the lungs known as pneumoconiosis. These particles are probably smaller than 1 micron and when lodged in the alveoli of the lung produce a low-grade inflammatory reaction and the appearance of dust-carrying phagocytes. Passing into the lymphatics, the dust cells tend to migrate along the lymphatics to the hilar nodes. If present in excessive amounts, they block lymph flow, with resulting localized lymphoid hyperplasia and fibrosis.⁵

In persons who are sensitized to pollens, inhalation of these air impurities precipitates symptoms of hay fever and pollen asthma. The concentration of pollen in the air varies greatly in different localities and is often enormous. In Chicago, for example, it has been shown that hundreds of tons of ragweed pollen are liberated each season.⁶

Many mechanical devices have been built for removing dusts from the air. However, because of the large variety of dusts, their difference in size and chemical composition and the varying conditions under which they are found, there is no single filtration method which is applicable to all.

The main object is to remove as nearly 100 per cent of the dust as is possible. To this end Rowley⁷ has

laid down a group of fundamental requirements for air filtering devices, namely:

1. High efficiency, or dust arresting power.
2. Low resistance to the flow of air through the filter.
3. High dust-holding capacity, or long life in service.
4. Economy in first cost and upkeep.
5. Freedom from odors.
6. Fire resistance.
7. Uniform efficiency over a wide range of air temperature.
8. Low moisture absorption.

Obviously these requirements must be modified to fit certain types of air cleaning, such as the water spray.

Air cleansing may be accomplished in numerous ways. In general the methods can be roughly grouped into five main divisions: air washers (water sprays), dry filters, viscous coated filters, electrical precipitators and dynamic precipitators.

The results obtained from any specific type of filtering method depend on specific properties of the filtering device and the operating conditions under which it is used and will vary over a wide range. Each method has a definite field of usefulness and when used within its own limitations attains its maximum efficiency.

In general it may be stated that dusts of small size which are harmful to health require filtration of the highest efficiency under the most variable conditions. In industry, the dynamic and electrical precipitators are perhaps the most efficient for the removal of the smaller particles of dust, whereas for home and hospital use dry filters are most efficient.

The air washer for the removal of dust and pollen from air does not have as high a degree of efficiency as other methods. Mechanically it is impossible to remove all fine dust particles from a stream of air with an air washer. Bubbling air through a volume of water at a slow rate, particularly if the water is greatly agitated by mechanical means, gives a higher degree of efficiency in dust removal than the air washer. The greatest field of usefulness of the air washer is as a primary cleaner in a system in which there is a secondary filter of greater efficiency. In this capacity it will remove the larger particles and thus give a longer life to the secondary filter in addition to maintaining or increasing the humidity.

Dry filters are made from felt, closely woven cloth, cotton mats and cellulose material (paper type). A filter of this type is spread on a frame, usually in a fluted fashion to give a large filtering surface to allow a slow seepage of air. Modern developments in this type of filtering medium permit large volumes of air to be passed through the filter without sacrificing efficiency. It is apparent that this type of filtering material is superior to water cleaning as well as viscous coated filters for the removal of dusts and pollens injurious to health. Such filters are well adapted for installation in hospitals and homes where filtration is required. Their efficiency is at its maximum when the filter is new. When properly cared for under ordinary operating conditions, the loss in efficiency of dry filters is very slight.

Viscous coated filters are made of numerous types of materials such as spun glass, metal wool or fibrous material, which are usually packed loosely in a frame or so arranged that the air is deflected from surface to surface. The material is coated with a thick viscid oil. The retention of dust is due to the fact that it sticks

1. Atmospheric Contamination, editorial, J. A. M. A. 110:1839 (May 28) 1938.

2. Bloomfield, J. J.: Outdoor Life 25:457, 1928.

3. Schrader, J. H.; Coblenz, M., and Korff, F. A.: Am. J. Pub. Health. 19:7, 1929.

4. Report of the Committee on Public Health of the New York Academy of Medicine, Bull. New York Acad. Med. 7:751, 1931. Yaglou, C. P.: Heating, Piping and Air Conditioning, 1931, p. 57; Physical and Physiologic Principles of Air Conditioning, J. A. M. A. 108:1708 (May 15) 1937; *ibid.* 109:945 (Sept. 18) 1937.

5. Funk, Elmer H.: Oxford Monographs on Diagnosis and Treatment 5:255, 1936.

6. Koessler, K. K., and Durham, O. C.: A System for an Intensive Pollen Survey, J. A. M. A. 86:1204 (April 17) 1926.

7. Rowley, Frank B.: Univ. Illinois Bull. 34:45 (Oct.) 1936.

to the oily surfaces and not that particles cannot pass through the openings. This type of filter has its lowest efficiency for dust arrestment when new, but as the filter fills with dust the efficiency increases.⁷

Electrical precipitators have lately been advocated for use in the removal of dust and pollen from the air. They maintain a high degree of efficiency for dust removal. The operating principle is not new in industry, where it is known as the Cottrell method. It consists of suspending a wire at a high potential below a series of plates which are oppositely charged. The dust particles are charged by the high potential wire and in passing over the plates are electrically attracted to them and stick there. This method is efficient for particles smaller than 0.5 micron. Its disadvantages for home and hospital use are that it may liberate ozone, which at times may produce secondary effects, and it requires constant operation to maintain its efficiency. If the unit is shut down, the particles which have become adherent to the plates lose their charge and may fall to the bottom of the ducts, and when operation of the unit is resumed these may be blown out in a large volume. The electrical filtering device therefore requires a supplementary filter when used in homes or hospitals. A filter to be used in homes or hospitals should be as foolproof as possible.

Dynamic precipitators usually combine an exhauster and dust collector in a single unit. There is a primary and secondary air passage and a turbine-like impeller composed of a large number of carefully calculated hyperboloid blades. The dust laden air is drawn into the unit by forces created by the rotating impeller; then the dust is separated and the cleaned air discharged. Dust drawn off by the impeller is directed through the secondary air circuit and collected in a hopper or passed outdoors. The dynamic precipitator has a very high degree of efficiency for dust removal as the result of the magnitude of the centrifugal and dynamic forces imparted to the dust particles by the impeller.

Within the past ten years, filtration of air for the removal of particulate matter has received a great deal of attention from the medical profession.⁸ This has been particularly true in the field of allergy. Its usefulness in the relief of symptoms of hay fever and pollen asthma and in other inhalant allergies as well as its value as an aid in diagnosis has been amply demonstrated.⁹ A brief survey of its value as shown by numerous workers may be summarized as follows: In uncomplicated hay

fever, residence of the patient in adequately filtered air will prevent the onset of symptoms due to sensitivity to pollens. Symptoms appear as soon as the person is exposed to pollen laden air. Persons experiencing symptoms due to pollen are relieved on entering a room with adequately filtered air, the length of time required for such relief depending on the severity of symptoms on entering. In a large series of observations, the average time required for maximum relief was found to be 1.2 hours.¹⁰ Residence in dust and pollen free air does not increase a person's resistance to pollen or dust, nor is it a cure for pollinosis or dust sensitivity.

Pollen asthma likewise will be relieved by residence in adequately filtered air, the length of time required for such relief varying greatly with the severity of the asthma and the duration of the attack. This time may vary from a few hours to several days or even weeks.¹¹ The subjective symptoms clear up more rapidly than do the objective symptoms. Persons who have pollen asthma remain free as long as they remain in filtered air, with certain exceptions. As has been shown,¹² atmospheric changes of wide amplitude may precipitate severe symptoms in persons with pollen asthma confined in adequately filtered air. However, the patients must first have been exposed to pollen. Other factors of air conditioning such as controlled humidity and temperature play a definite role in the relief of pollen asthma. It has been observed that the rapidity with which persons who have pollen asthma are relieved is greater under conditions of low humidity and relatively constant temperature in pollen free atmosphere than when the temperature and humidity are not controlled.¹³ In such controlled atmospheres, attacks of asthma precipitated by storms were apparently delayed from six to eight hours and were less severe than those observed when humidity and temperature were not controlled.¹³

Residence in adequately filtered air is a procedure of great help in the diagnosis of allergic conditions. The effect of dusts, pollens and other inhalant factors usually may be ruled out in a few days by this method.

In other respiratory conditions which are definitely attributed to the effect of dust such as pneumoconiosis, the use of air filtration for removal of dusts is now a recognized preventive measure. Many industries, realizing the benefits derived by the employees from such treatment of the air, have installed devices for the removal of dust.¹⁴

Air conditioning is recognized as most essential in many manufacturing processes, as for example in the production of rayon, photographic film, capsules, candy,

8. Taylor, T. A., and Taylor, W. H.: *Anesth. & Analg.* **13**: 22 (Jan.-Feb.) 1934. Linke, F.: *Ztschr. f. d. ges. Krankenhausw.*, Oct. 30, 1934, p. 509. Beach, B. S.: *Scient. Am.* **157**: 152 (Sept.) 1937.

9. This work has been described in the articles listed in footnote 11 and also in the following:

Storm van Leeuwen, W.: *Proc. Roy. Soc., Section of Therapeutics and Pharmacology*, part 3, **17**: 19 (April) 1924.
Storm van Leeuwen, W.: *München. med. Wchnschr.* **77**: 726, 1930.
Leopold, S. S., and Leopold, C. S.: *Bronchial Asthma and Allied Allergic Disorders*, J. A. M. A. **84**: 731 (March 7) 1925.
Cohen, M. B.: *M. J. & Rec.* **123**: 322 (March 3) 1926.
Peshkin, M. M., and Beck, L.: *J. Lab. & Clin. Med.* **15**: 643 (April) 1930.
Storm van Leeuwen, W., *ibid.* **16**: 442 (Feb.) 1931.
Gay, L. N.: *The Treatment of Hay Fever and Pollen Asthma by Air-Conditioned Atmosphere*, J. A. M. A. **100**: 1382 (May 6) 1933.
Griebel, C. R.: *Ztschr. f. Laryng., Rhin. & Otol.* **24**: 207, 1933.
Rowe, A. H.: *M. J. & Rec.* **138**: 345 (Nov. 15) 1933.
Vaughan, W. T., and Cooley, L. E.: *J. Allergy* **5**: 37 (Nov.) 1933.
Kahn, I. S., and Grothaus, E. H., *ibid.* **5**: 45 (Nov.) 1933.
Kendal, T. A., and Weidner, G.: *Heating, Piping and Air Conditioning*, February 1934, p. 75.
Davies, C.: *M. J. & Rec.* **129**: 543 (May 16) 1934.
Habettin, P.: *Wien. klin. Wchnschr.* **47**: 651 (May 25) 1934.
Crip, L. H., and Green, M. A.: *J. Allergy* **7**: 120 (Jan.) 1936.
Crip, L. H.: *Mod. Hosp.* **46**: 82 (June) 1936.
von Neergaard, K.: *Balnearologie* **3**: 386 (Aug.) 1936.
von Neergaard, K.: *Schweiz. med. Wchnschr.* **66**: 837 (Aug. 29) 1936.
Welker, W. H.: *Univ. Illinois Bull.* **34**: 15 (Oct.) 1936.
Fraenkel, E. M.: *Proc. Roy. Soc. Med.* **30**: 1547 (Oct.) 1937.
Voss, O.: *Beitr. z. Klin. d. Tuberk.* **89**: 311, 1937.

10. Rappaport, B. Z.; Nelson, Tell, and Welker, W. H.: *Effect of Air Filtration in Hay Fever and Pollen Asthma*, J. A. M. A. **98**: 1861 (May 28) 1932.

11. Reported in the following articles:
Cohen, M. B.: *Clin. Med. & Surg.* **34**: 276 (April) 1927; *J. Lab. & Clin. Med.* **12**: 59 (Oct.) 1927, 963 (July) 1928.

Kahn, I. S., in discussion on Cohen: *J. Lab. & Clin. Med.* **13**: 963 (July) 1928.

Rappaport, Nelson and Welker, footnotes 10 and 12.
Nelson, Tell, Rappaport, B. Z.; Canar, A. G., and Welker, W. H.: *Heating, Piping and Air Conditioning* **6**: 329 (Aug.) 1934.

Rappaport, Nelson and Welker.
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Nelson, Tell, Rappaport, B. Z., and Welker, W. H.: *Chicago Purchaser* **13**: 28 (June) 1935.

Ward, C. E.: *Proc. Staff Meet., Mayo Clin.* **11**: 609 (Sept. 23) 1936.
Trasoff, Abraham, and Blumstein, George: *J. Lab. & Clin. Med.* **22**: 147 (Nov.) 1936.

12. Nelson, Tell, Rappaport, B. Z., and Welker, W. H.: *The Effect of Air Filtration in Hay Fever and Pollen Asthma*, J. A. M. A. **100**: 1385 (May 6) 1932.

13. Rappaport, B. Z.; Nelson, Tell, and Welker, W. H.: *J. Allergy* **6**: 111 (Jan.) 1935.

14. Hatch, Theodore; Warren, Henry, and Kelley, G. S.: *J. Indust. Hyg.* **14**: 246 (Sept.) 1932. Hatch, Theodore; Fehnel, J. W.; Warren, Henry, and Kelley, G. S.: *ibid.* **15**: 41 (Jan.) 1933. Hatch, Theodore; J. Indust. Hyg. & Toxicol. **18**: 595 (Nov.) 1936. Price, C. W.: *Proc. Roy. Soc. Med.* **30**: 1544 (Oct.) 1937.

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

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SATURDAY, OCTOBER 1, 1938

THE FOOD, DRUG AND COSMETIC ACT BEGINS TO FUNCTION

The month of July witnessed the beginning of enforcement of the Federal Food, Drug and Cosmetic Act of 1938. While the majority of the provisions of the act will not become effective until next June, dangerous drugs and dangerous cosmetics are immediately subject to the new law. Moreover, the provisions concerning the introduction of new drugs are also in effect.

The American Medical Association took an active part in procuring the enactment of the Federal Food and Drugs Act of 1906, which in its final form was obviously inadequate to accomplish the purposes for which it was intended. The Association has cooperated and is cooperating to the extent of its ability in bringing about the enforcement of that act and of its several amendments, and through THE JOURNAL, the Bureau of Investigation and its Councils has endeavored to keep the public and the profession informed about many harmful, deleterious or unscientific preparations. The Association proposes to follow the same policy with respect to the new act.

Although the present act is not nearly perfect, it has removed certain restrictions; the government may now proceed to act against products not previously within the purview of the law. Many years ago the Bureau of Investigation published a report on irrational or other dangerous cosmetic preparations for dyeing eyebrows and eyelashes. One particularly (Lash Lure) was reported to contain the dangerous paraphenylenediamine mixture. THE JOURNAL called attention to cases of blindness which followed the use of this preparation by some persons. The Food, Drug and Cosmetic Administration of the United States Department of Agriculture in its report for the month of July states that it has proceeded against "Lash Lure" and other similar preparations. The manufacturer of "Lash Lure" has notified the administration through its attorney that it was ceasing shipments immediately.

Physicians not long ago were urged to the use of a product called Causalin. THE JOURNAL pointed out its

deficiencies and more recently a critical report¹ was issued by the Council on Pharmacy and Chemistry. In this report the Council indicated that Causalin was apparently a mixture containing an aminopyrine preparation and a derivative having chemical resemblance to cinchophen. Now the firm has been cited by the government because, the government alleges, the subsidiary label statement "Aminodimethyl-pyrazolon-Quinoline-sulphonate" was a false representation of the composition of the medicine, since other significant ingredients were present. The government alleges that the product, a pain-relieving preparation, is dangerous to health when used in dosages or with the frequency prescribed, recommended and suggested in the labeling.

Of much interest to physicians is the recent ruling of the Food and Drug Administration on sulfanilamide. Under the dangerous drugs provision of the new Food, Drug, and Cosmetic Act sulfanilamide is prohibited from being sold to the public in "patent medicines" so far as:

It is the consensus of qualified experts that sulfanilamide is a valuable aid in the treatment of several serious disease conditions when the dosage is properly adjusted to the requirement of the individual patient and frequency of dosage and duration of treatment are intelligently and expertly directed. It is further the consensus of such experts that, when used under other conditions, it is a dangerous drug, capable of causing serious injury and even death.

In the light of these facts, careful consideration has been given to the status of sulfanilamide under the provisions of the Food, Drug and Cosmetic Act which deals with traffic in dangerous drugs.

Sulfanilamide and drug preparations containing sulfanilamide or related compounds for indiscriminate use by the general public, in a manner which constitutes a serious danger to health, are, when found in interstate commerce, actionable, in the opinion of the Food and Drug Administration, under section 502 (j) of the Federal Food, Drug and Cosmetic Act, which section of the law is now in effect.

Similar ruling has been made for aminopyrine, for cinchophen and for neocinchophen.

Another item in the report of the Food and Drug Administration for the month of July refers to an investigation of a number of food products. Among them was a consignment of curry powder heavily contaminated with lead. Among the allegations made was that against 577 cans of a malted milk food drink containing little or no malted milk; 19,062 pounds of a so-called cocoa containing at least 12 per cent added vegetable gum; 426 packages of butter cookies containing little or no butter; 19 gallons of so-called lemon juice, found to be an imitation; 150 gallons of refined soy bean oil which was found to be 90 per cent mineral oil; a sizable quantity of horseradish made up entirely of parsnips flavored with mustard oil and vinegar, and 104 sacks of caraway seed from which nearly all the essential flavoring oil had been distilled.

The Food and Drug Administration continued its campaign of confiscation against unsterile gauze bandages and absorbent cotton, of which there seems to be

1. Causalin (Causyth) Not Acceptable for N. N. R., J. A. M. A. 109:506 (Aug. 14) 1937.

a profuse amount on the market. Among other confiscations were sixty bottles of milk of magnesia with cascara and sixty-three bottles of milk of magnesia with vanilla and sugar, both failing to conform to their label claims of composition.

The Federal Trade Commission also has serious responsibilities in the regulation of advertising to the public. Recently it issued a release in which it is indicated that the U. S. District Court of Chicago has issued an order temporarily restraining the Hartman chain of drug stores from disseminating in any manner false advertisements concerning a weight reducing compound. The bill of complaint alleges that the defendant has falsely advertised the product for the purpose of inducing, or as a product which is likely to induce, its purchase as a weight reducer. According to the complaint the advertisement is false. Not only is the product not widely prescribed by practicing physicians, but also the advertisement fails to reveal that the use of this product under the conditions recommended may be injurious to the health of the user by causing loss or serious impairment of eyesight. It was brought out that the active ingredient in the drug is known as dinitrocresol. This is essentially similar in action to dinitrophenol. An affidavit by Dr. Harry Gradle states that he treated a Chicago woman suffering from a cataract of each eye following the use of the nostrum. *THE JOURNAL* and the Council on Pharmacy and Chemistry have frequently warned against the use of the nitrophenol type of weight reducing preparations.

The medical profession will follow with interest the further work of the Food and Drug Administration and the Federal Trade Commission since they have been fortified with new laws to combat deception. Some time may elapse before the courts will pass judgment on the new laws; until this is done their exact status will not be known. The medical profession will always be found solidly with the government in its protection of the public against the exploiters of impure or harmful foods, drugs and cosmetics.

PROTRUDED INTERVERTEBRAL DISK, BACK PAIN AND SCIATICA

Medical periodicals of the past few years contain a number of contributions dealing with the rupture of the intervertebral disk and its herniation into the spinal canal as a cause of intractable back pain and sciatica. The center of interest for the student of these conditions seems to have shifted from spondylolisthesis to the rupture of the nucleus pulposus. The exact knowledge of the anatomy and embryology of this long neglected structure dates back to the anatomic studies of von Luschka (1858). A correct clinical or pathologic approach to the subject of the intervertebral disk, however, is a recent contribution, the result of the accurate and painstaking necropsy studies of the Dresden pathologist Schmorl.

Briefly the intervertebral disk consists of an outer dense fibrocartilage firmly attached to the adjacent vertebrae and forming a strong but elastic ring, annulus fibrosus or lamellosus, acting as an envelop for the interior semifluid mass of fibrogelatinous pulpy center, the nucleus pulposus. The firm fluid cushion or shock absorber is subject, as pointed out by Keyes and Compere,¹ to the laws of fluids. It is incompressible and confined to its normal shape and position by the strong and elastic annulus fibrosus. The amount of compression of the intervertebral disk will therefore depend on the elasticity and strength of the annulus fibrosus. The incompressibility of the nucleus pulposus lends to it the function of transmitting the static and muscular forces from one vertebra to the next and establishes it as the axis of motion on which each vertebral body must work.

Schmorl found in his necropsy studies of the spine that the intervertebral disk is often involved in pathologic changes, the most common being prolapse (38 per cent) of the nucleus pulposus into the spongiosa of the adjacent vertebra, leading later to the formation in the involved vertebra of the so-called Schmorl nodules. He discovered further that in about 15 per cent there were small posterior prolapses of the nucleus pulposus beneath the posterior longitudinal ligament but concluded that they rarely, if ever, produced clinical symptoms. He advanced the concept of the rupture of the nucleus pulposus as the starting point for a number of pathologic changes in the spine, the rupture being facilitated or caused by the degenerative changes in the annulus fibrosus, with mild trauma as a second factor.

The earliest clinical report of this condition was that of Goldthwaite, who reported a case of sciatica and paraplegia due to a posterior herniation of the intervertebral disk at the lumbosacral junction. He suggested that such displacements might be the cause of many cases of sciatica, lumbago and back strain. A similar case was reported by Middleton and Teacher of England, but both observations attracted little interest. In the next decade and a half, a number of neurosurgeons, among them Elsberg, Stookey, Bucy, Adson and Dandy, reported cases of enchondroma developing from the intervertebral disk and causing spinal cord compression. In 1934 Mixter and Barr² reported from the Massachusetts General Hospital a series of nineteen cases of rupture of the disk, establishing it as a clinical entity and a cause of intractable back pain and sciatica. In 1935 Mixter and Ayer³ added observations on fifteen more cases. In *THE JOURNAL*, Love and Walsh⁴ have reported 100 cases in which the protruded inter-

1. Keyes, D. C., and Compere, E. L.: The Normal and Pathological Physiology of the Nucleus Pulposus of the Intervertebral Disk, *J. Bone & Joint Surg.* **14**: 897 (Oct.) 1932.

2. Mixter, W. J., and Barr, J. S.: Rupture of the Intervertebral Disk with Involvement of the Spinal Canal, *New England J. Med.* **211**: 210 (Aug. 2) 1934.

3. Mixter, W. J., and Ayer, J. B.: Herniation of Rupture of the Intervertebral Disk into the Spinal Canal, *New England J. Med.* **213**: 385 (Aug. 29) 1935.

4. Love, J. G., and Walsh, M. N.: Protruded Intervertebral Disks, *J. A. M. A.* **111**: 396 (July 30) 1938.

vertebral disk was removed at operation. It appeared that the enchondromas of the earlier reports were in reality prolapsed nuclear material impinging on the cord, cauda equina, nerve routes or posterior longitudinal ligament. The favorite location is the lower lumbar region, probably because it is subjected to the greatest mechanical stress in heavy lifting or pushing.

The clinical diagnosis of a protruding disk as the cause of sciatica is based, according to Love and Walsh, on a history of trauma to the back with persistent or recurrent low back and sciatic pain, with diminished or absent achilles reflex, and an increased total protein content of the cerebrospinal fluid. The diagnosis is confirmed and the protruded disk identified by fluoroscopic examination of the spinal canal after the subarachnoid injection of iodized oil through a lumbar puncture needle. If on examination of the movements of the opaque oil in the spinal canal a persistent defect characteristic of protruded disk is observed, and if a lesion located at that level could account for the patient's pain, surgical removal of the protruded portion of the disk is indicated. Barr⁵ has reported that fifty-four patients of fifty-eight operated on were either well or markedly improved, and Love and Walsh state that there has not been a single recurrence in their series of 100 cases. The incidence of this entity is unknown. According to Barr, 90 or 95 per cent of the patients who have sciatica recover either spontaneously or after conservative treatment and do not need to be subjected to the highly technical and possibly dangerous examination with iodized oil. It is well, perhaps, to heed his admonition that there is some danger that too many patients will be subjected to examination with iodized oil or to radical exploratory surgery as a result of the untempered enthusiasm of certain men who assume that this entity is the cause of all sciatica.

Current Comment

ASCITIC FLUID TRANSFUSION

Davis and White¹ of the Department of Surgery, George Washington University School of Medicine, have reported recently that human ascitic fluid may be successfully substituted for whole blood in transfusion. Ascitic fluid has the advantage of low cost, as a constant source of supply is present in every hospital. The fluid is readily maintained in a sterile condition and does not deteriorate on storage. While their conclusions are based solely on experiments with transfusion in dogs, they see no reason why their results should not be equally applicable to man. Various substitutes for whole blood have been suggested and tried in transfusion. Gum-saline and gelatin-saline solutions were extensively used during the World War. More recent tests have been with hemoglobin Ringer's solution, or with whole blood or plasma obtained from the placenta, umbilical

cord or cadaver. In their attempt to find a less objectionable substitute, the Washington surgeons withdrew peritoneal exudate from patients suffering from cardiac decompensation or portal cirrhosis. The fluids were filtered through gauze and stored without preservative at 5 C. for varying periods up to five months. Bacteriologic examinations made at intervals by the blood-agar plate method showed that the fluids were sterile. Compatibility tests with the blood of the prospective canine recipients were made before transfusion. The dogs weighed from 7 to 10 Kg. and were given pentobarbital sodium anesthesia. Shock was induced in these dogs by the gradual withdrawal of about 350 cc. of arterial blood. The average initial blood pressure (kymograph tracing), about 150 mm. of mercury, was reduced to about 55 mm. by this bleeding. About 500 cc. of ascitic fluid was warmed to 33 C. and allowed to flow into the femoral vein at the rate of 15 cc. per minute. As a result of this ascitic transfusion the carotid pressure was raised to 120. The animals survived indefinitely and did not show immediate or delayed transfusion toxicity. Albuminuria, glycosuria or hematuria was never observed. Whether or not retransfusion after an incubation period of from three to five weeks would produce retransfusion shock was not tested. The possibility of evaporating the ascitic fluid to dryness and redissolving before transfusion has not yet been tried.

EFFECT OF INSULIN IN VITRO

One of the most important of the unsolved problems in the biologic sciences is the mechanism of the action of insulin. The injection of insulin promotes the oxidation of carbohydrate but the exact mode of action of the hormone in stimulating these processes is not certain. The many physiologic variables present in the organism have made it extremely difficult to separate the processes involved in the action of insulin, even though the effects of the hormone have been rather completely postulated from work on the intact diabetic organism. Many efforts have been made to simulate the results of the activity of insulin by a large variety of in vitro experiments. The complete description of the mode of insulin action would no doubt greatly increase the amount of available information regarding carbohydrate metabolism and might perhaps also indicate how intimately the oxidation of fatty acids is related to the simultaneous combustion of carbohydrate. Past work has, however, yielded for the most part essentially negative results. The importance of the problem increases the significance of a recent article¹ describing an effect of insulin on oxidations in isolated muscle tissue. In a study of the respiration of minced pigeon breast muscle, in the Warburg apparatus, it has been demonstrated that the addition of insulin retards the decline in respiration, which under these conditions ordinarily begins from half an hour to an hour after the initiation of the experiments. The falling off in the respiration is also inhibited by the addition of citrate or certain compounds derived from citrate (succinate, fumarate) all of which have been postulated as inter-

5. Barr, J. S.: The Relationship of the Intervertebral Disk to Back Strain and Peripheral Pain (Sciatica), *Surgery* 4:1 (July) 1938.
1. Davis, H. A., and White, C. S.: *Proc. Soc. Exper. Biol. & Med.* 38: 462 (May) 1938.

1. Krebs, H. A., and Eggleston, L. V.: *Biochem. J.* 32:913 (May) 1938.

mediates in the biologic oxidation of carbohydrates.² Particularly noteworthy is the fact that insulin has its greatest effect if added together with citrate and muscle extract, and it is therefore concluded that insulin acts as a catalyst in a "citric acid cycle".² The exact significance of these results cannot be determined until many more experimental data have become available. The observations are perhaps most noteworthy because of the finding of a positive effect for insulin. It should be pointed out, however, that the quantities of insulin required to demonstrate this in vitro action are approximately twenty times greater than the amounts required to produce an effect in the intact organism. Quite likely the entire mechanism of the action of insulin is not attributable to a single primary stimulation of the oxidation of carbohydrate. Nevertheless the results suggest the possibility of demonstrating in vitro other primary effects of insulin on carbohydrate metabolism.

Association News

ABSTRACT OF MINUTES OF MEETINGS OF BOARD OF TRUSTEES HELD IN CHICAGO, SEPT. 15-17, 1938

Meetings of the Board of Trustees were held on Thursday, Friday and Saturday of the week of the special session of the House of Delegates, and the following actions were taken:

ST. LOUIS SESSION

May 15-19, 1939, was the date set for the St. Louis session of the Association, and the nomination by the St. Louis Medical Society of Dr. Robert E. Schlueter as chairman of the Local Committee on Arrangements was confirmed.

APPOINTMENTS

Drs. George Blumer and Paul J. Hanzlik were reappointed on the Committee on Scientific Exhibit for a period of three years.

Drs. William P. Wherry, Paul Titus, John R. Neal, Charles B. Pinkham, S. S. Goldwater, Malcolm T. MacEachern, Donald Balfour and Alan M. Chesney and Rev. Alphonse M. Schwitalla were elected to constitute an Advisory Committee to the Council on Medical Education and Hospitals.

APPROPRIATIONS

Appropriations were made for special exhibits on anesthesia and fractures for the St. Louis session of the Association; for an investigation by the Council on Foods of the lead content of certain foods, particularly products used in infant feeding, and for the expansion of the public relations activities of the Association.

PUBLICATION OF BOOKS

Authorization was given for the printing of a limited edition of the manual for periodic health examinations to meet current needs, and for the development of a new manual. Permission also was granted for the reprinting in book form, in English and in Spanish, of the series of articles on vitamins which appeared in THE JOURNAL.

POSTPONEMENT OF CONFERENCE ON MEDICAL PATENTS

Because of preparations for conferences and meetings that were not previously contemplated, it has been difficult to carry out the plan of calling a conference on medical patents early in the fall. This matter will be given further consideration at the November meeting of the Board.

MISCELLANEOUS

Numerous other matters received consideration, and many of these will be acted on at a later date.

2. Krebs, H. A.; Salvin, Ernest, and Johnson, W. A.: *Biochem. J.* 32: 113 (Jan.) 1938.

FORMER DELIBERATIONS

Appointments: The following appointments were made at the former meeting of the Board, and acceptances have been received:

Dr. Russell Haden to succeed Dr. L. R. Thompson as the Association's representative on the Division of Medical Sciences of the National Research Council for a period of three years.

Dr. Irvine McQuarrie to succeed Dr. Grover T. Powers on the Council on Foods.

Dr. Edmund V. Cowdry to succeed Dr. George W. Churchman on the Commission on Standardization of Biological Stains.

Drs. L. D. Bristol, A. J. Lanza and C. D. Selby as additional members of the Council on Industrial Health.

Dr. W. W. Bauer to serve on Joint Committee on Nursing Service.

Dr. Morris Fishbein to represent the Association on the Joint Committee to Investigate the Problems of Indexing and Abstracting Services in the Major Fields of Research proposed by the American Library Association.

Drs. Allen H. Bunce, Thomas S. Cullen and Roger I. Lee to constitute the Committee on Scientific Exhibit.

RADIO BROADCASTS

The fourth series of programs broadcast in dramatic form portraying fictitious but typical incidents of significance in relation to health by the American Medical Association and the National Broadcasting Company entitled "Your Health" will begin Wednesday, October 19, and run consecutively for thirty-six weeks. The program will be broadcast over the Blue network of the National Broadcasting Company each Wednesday at 2 p. m. eastern standard time (1 p. m. central standard time, 12 noon mountain time, 11 a. m. Pacific time).

These programs will be broadcast on what is known in radio as a sustaining basis; that is, the time is furnished gratis by the radio network and local stations and no revenue is derived from the programs. Therefore, local stations may or may not take the program, at their discretion, except those stations which are owned and operated by the National Broadcasting Company.

The program to be broadcast in the first group, together with their dates and their topics, are as follows:

October 19. What Is Health?
October 26. Growing Strong.
November 2. Seeing and Hearing Well.
November 9. Healthier Boys and Girls.

The following is a list of the stations connected with the Blue network of the National Broadcasting Company, but no assurance can be given as to how many of these stations will broadcast the program "Your Health":

Basic Blue Network

WJZ	New York	WEBR	Buffalo	KSO	Des Moines
WBZ	Boston	KDKA	Pittsburgh	KOIL	Omaha
WBZA	Springfield	WHK	Cleveland	WREN	Kansas City
WEAN	Providence	WSPD	Toledo	WLW	Cincinnati
WICC	Bridgeport	WXYZ	Detroit	WCKY	Cincinnati
WFIL	Philadelphia	WOVO	Fort Wayne	WSAI	Cincinnati
WBAL	Baltimore	WENR-WLS	Chicago	WRTD	Richmond
WMAL	Washington	KWK	St. Louis	WBAB	Albany
WSYR	Syracuse	WMT	Cedar Rapids	WJTN	Jamestown, N.Y.
WHAM	Rochester	WTCN	Minneapolis-St. Paul	WLEU	Erie

Supplementary Facilities

WFEA	Manchester, N. H.	WFBC	Greenville	KVOD	Denver
WBRE	Wilkes-Barre	WWNC	Asheville	KLO	Ogden
WSAN	Allentown, Pa.	WIS	Columbia	KIDO	Boise
WORK	York, Pa.	WCSC	Charleston	KGIR	Butte
WCOL	Columbus, O.	WJAX	Jacksonville	KPFA	Helena
WGL-WOVO		WFLA-WSUN	Tampa	KGHL	Billings
	Ft. Wayne	WIOD	Miami	KSEI	Pocatello, Ida.
WOOD	Grand Rapids	WMC	Memphis	KTFI	Twin Falls, Ida.
WBOV	Terre Haute	WSB	Atlanta	KGO	San Francisco
WGBF	Evansville	WBRC	Birmingham	KECA	Los Angeles
WBCB	Duluth-Superior	WJDX	Jackson	KEX	Portland, Ore.
KSOC-KELO		WSMB	New Orleans	KJR	Seattle
	Sioux Falls, S. D.	WALA	Mobile	KGA	Spokane
KANS	Wichita	WROL	Knoxville	KFBK	Sacramento
WTAR	Norfolk	WAVE	Louisville	KWG	Stockton
WPTF	Raleigh	WSM	Nashville	KMJ	Fresno
WSOC	Charlotte	WTMJ	Milwaukee	KERN	Bakersfield
		WIBA	Madison		

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ALABAMA

Regional Meetings.—The fall meeting of the Northeastern Division of the Alabama State Medical Association was held September 22 in Anniston. Among the speakers were Drs. James N. Baker, Montgomery, state health officer, on "Future Plans and Needs of the State Department of Health"; Seale Harris, Birmingham, "Gastrointestinal Symptoms and Management of Pellagra"; John W. Boggess Jr., Guntersville, "Some Clinical Observations in Asthmatic Cases"; Charles N. Carraway, Birmingham, "Intravenous Sodium Pentothal and Oxygen Anesthesia"; Bishop B. Warwick, Talladega, "Nasal Headaches" and Jerre Watson, Anniston, "Some Errors in Diagnosis."—At a meeting of the Southeastern Division in Dothan August 11 the speakers were Drs. Gordon R. Smith, Ozark, on "Treatment of Chronic Ulcers"; Hugh Dent Johnson, Montgomery, "Modern Management of Acute Intestinal Obstructions"; Clarence R. Bennett, Eufaula, "Coma and Its Differential Diagnosis"; Archie E. Thomas, Montgomery, "Treatment of Syphilis in Pregnancy," and John L. McGehee, Memphis, Tenn., "Use of Living Fascial Transplants in Repair of Certain Types of Hernia."

ARIZONA

Harlow Brooks Navajo Clinical Conference.—The third Harlow Brooks Navajo Memorial Clinical Conference was held at the Sage Memorial Hospital, Ganado, August 29-31. Louis H. Evans, D.D., Pittsburgh, president, Board of National Missions, Presbyterian Church, gave the welcoming address. In addition to clinics, the following papers were presented:

- Dr. Philip Lee Travers, Gallup, N. M., The Development of the Work of Sage Memorial Hospital and the Harlow Brooks Memorial Navajo Clinical Conference.
- Dr. Bowman C. Crowell, Chicago, Bone Sarcoma.
- Dr. Carl F. Rusche, Los Angeles, Urinary Extravasation.
- Dr. John H. Patterson, Phoenix, Local Anesthesia in Major Surgery.
- Dr. Grover C. Penberthy, Detroit, Management of Certain Lesions of the Esophagus.
- Dr. William H. Daniel, Los Angeles, Proctology for the General Practitioner.
- Dr. Fred H. Albee, New York, Reconstruction Surgery of the Skeleton.
- Dr. Charles H. Arnold, Lincoln, Neb., Surgical Treatment of Nephrophtosis.
- Dr. Joseph Madison Greer, Phoenix, Observations on Another Method of Pinning Fractures of the Neck of the Femur.
- Dr. E. Payne Palmer, Phoenix, A Plea for an Early Diagnosis and Radical Treatment of Gastric Carcinoma.
- Dr. Victor S. Randolph, Phoenix, Bronchography in Diagnosis of Pulmonary Disease.

ARKANSAS

District Meeting.—The Tenth Councilor District Medical Society held a meeting in Fort Smith September 20 with the following speakers, among others: Drs. Ira F. Jones, Fort Smith, on "Differential Diagnosis Between Gastric and Duodenal Ulcer from the Standpoint of the General Practitioner"; William R. Brooksher, Fort Smith, "Present Status of Irradiation Therapy in Breast Tumors" and Herman W. Hundling, Little Rock, "Diverticulitis of the Sigmoid." Clinics were held at Sparks Memorial and St. Edward's Mercy hospitals.

New Cancer Foundation.—The Elise A. Lake Foundation has been organized within the past year to cooperate with the free cancer clinic of the University of Arkansas School of Medicine, Little Rock. The foundation is sponsored by the Arkansas Federation of Women's Clubs and is named in honor of the late Mrs. Elise A. Lake, Hot Springs, a past president of the federation, who for a year or more before her death was active in a statewide educational campaign for the early diagnosis of cancer. Its object "shall be mutual counsel and helpfulness in uniting the influence and service of citizens of the state, in promoting education for early diagnosis and treatment of cancer and to raise funds for the Elise A. Lake Foundation to increase facilities for diagnosis and treatment of cancer" at the university cancer clinic. The foundation is now seeking funds to carry out its work and county units are being organized. At a dinner during the biennial convention of the federation of women's clubs in May, pledges and cash amounting to about \$1,200 were received. Mr. Lake, who was

named honorary chairman, had previously given the foundation its first pledge of \$1,000. Mrs. John F. Weinmann, Little Rock, is chairman. The late Dr. Harvey Thatcher, professor of pathology at the university medical school, was active in the organization of the foundation, and his successor, Dr. Albert F. De Groat, is now vice chairman. Physicians on the advisory council are Drs. Frank Vinsonhaler, dean of the medical school; Joy K. Donaldson, associate professor of surgery, and William B. Grayson, Little Rock, state health officer.

DELAWARE

State Medical Meeting.—The one hundred and forty-ninth annual meeting of the Delaware State Medical Society will be held in Dover at the New State House October 11-12, under the presidency of Dr. Clarence J. Prickett, Smyrna. Guest speakers will be:

- Dr. Isidor S. Ravdin, Philadelphia, Surgical Problems of Hyperthyroidism.
- Dr. Maurice C. Pincoffs, Baltimore, Arterial Hypertension.
- Dr. Edward A. Schumann, Philadelphia, The Classic Cesarean Section.
- Dr. Lawson Wilkins, Baltimore, Hypothyroidism in Children.
- Dr. Francis G. Harrison, Philadelphia, Blood Stream Infections in Urologic Cases.
- Dr. Richard A. Kern, Philadelphia, Clinical Allergy.
- Dr. David A. Cooper, Philadelphia, Indications for Surgery in the Treatment of Pulmonary Tuberculosis.
- Dr. Thomas M. McMillan, Philadelphia, The Problem of Heart Disease as It Stands Today.
- Drs. Kenneth E. Appel and James A. Flaherty, Philadelphia, Modern Trends in Psychiatric Therapy.
- Dr. Raymond A. Vonderlehr, U. S. Public Health Service, Washington, D. C., Present Day Control of Venereal Diseases from a State and National Viewpoint.
- Dr. Bernard P. Widmann, Philadelphia, The Status of X-Ray and Radium in Treatment of Cancer.

Dr. Morris Fishbein, Chicago, Editor of THE JOURNAL, will deliver a public address Wednesday evening October 12 on "The National Health Program and American Medicine."

ILLINOIS

New County Sanatorium.—A tuberculosis sanatorium for Lake County is to be built near Waukegan with a PWA grant of \$193,091 and a fund of \$233,000 to be raised through a bond issue and a tax levy, *Hospital Management* reports. The sanatorium will have a capacity of ninety-two beds. There will also be a nurses' home and a physicians' residence.

Chicago

Golf Tournament.—Dr. August F. Daro was the first winner of the new Chicago Medical Society Championship Trophy, which is to be awarded annually to the champion in the annual golf tournament. Dr. Daro tied with Dr. Homer K. Nicoll with a score of 78 at the tournament at the Olympia Fields Country Club August 31 and the tie was played off at the North Shore Country Club September 18, with Dr. Daro the winner. Dr. Grover E. Johnson won the VanDerSlicke Trophy with a gross score of 79 and Dr. Harry E. Mock the Sisson Trophy for low net with a score of 32-63-95.

New Research Building for Abbott Laboratories.—The fiftieth anniversary of the founding of Abbott Laboratories, pharmaceutical manufacturers, in North Chicago, will be celebrated October 7 with the dedication of a new laboratory building. There will be a special program in the building in the afternoon following an inspection tour in the morning. The speakers will be:

- Karl T. Compton, Ph.D., president, Massachusetts Institute of Technology, Cambridge, Mass., The University and the Public Welfare.
- Dr. Herbert M. Evans, Berkeley, Calif., professor of anatomy, Morris Herstein professor of biology, and director of the Institute of Experimental Biology, University of California Medical School, The Task and Spirit of Research.
- Dr. Thomas Farrar, surgeon general, U. S. Public Health Service, Washington, D. C., Research and Public Health.

In the evening a program will be presented at the Palmer House with the following speakers:

- Harrison E. Howe, Sc.D., Washington, D. C., editor, *Industrial and Engineering Chemistry*, The Contributions of Organized Chemistry.
- George D. Beal, Ph.D., assistant director, Mellon Institute, Pittsburgh, The Scientific Development of Drug Standards.
- Dr. Morris Fishbein, Chicago, Editor, THE JOURNAL, The Contributions of Medicine to the Public Welfare.

The new building is three stories high with an attic and basement, providing facilities for the chemical, bacteriologic, botanic, medical and pharmaceutical research activities of this firm. In addition to laboratories it contains a micro-analytic laboratory, a library with accommodation for 20,000 volumes, hot and cold rooms for stability studies, dark rooms on each floor for the use of optical instruments, one dark room for use as a laboratory for light sensitive reactions, and an air conditioned auditorium seating 800 persons.

INDIANA

Courses in Obstetrics.—Plans are under way to offer two week courses in obstetrics regularly throughout the year for Indiana physicians under the auspices of the department of obstetrics of Indiana University School of Medicine, Indianapolis, cooperating with the Indiana State Medical Association. It is planned to offer to four physicians at each session an intensive study in obstetrics and pediatrics. While attending the courses, the physicians may reside at the Coleman Hospital at the Indiana University Medical Center. There will be no charge for maintenance or tuition during the two week period.

City Receives Cancer Clinic.—The city of Indianapolis was formally presented August 18 with the new cancer clinic at the city hospital known as Patrick Hall. Edwin L. Patrick, Indianapolis business man, made the presentation; Mayor Walter C. Boetcher accepted the clinic, in turn presenting it to Dr. George W. Kohlstaedt, president of the city board of health. The cancer clinic is the gift of the late Mrs. Kathryn Cones Patrick, who in leaving a \$100,000 benefaction fund stipulated that her husband was to select the recipient. The new department, which offers complete equipment for the treatment of cancer, will be maintained from the income of a fund of \$60,000; \$40,000 of the original sum was used for equipment.

LOUISIANA

Society News.—The Tri-Parish Medical Association was addressed in Tallulah August 9 by Drs. John G. Snelling, Monroe, on "Medical and Surgical Aspects of Thrombocytopenic Purpura"; Dr. Arthur A. Herold, Shreveport, "A Story of Diabetes Mellitus with Evaluation of Present Day Treatment," and James B. Vaughn, Monroe, "The Reasons for the Change in Medical Economics."—The Bi-Parish Medical Society was addressed at the East Louisiana State Hospital, Jackson, August 3, by Drs. Isidore Cohn and Eugene B. Vickery, New Orleans, on "Vascular Clinics" and "Diagnosis and Treatment of Renal Diseases, with Some of the Newer Drugs with Results" respectively.—At a meeting of the Tangipahoa Parish Medical Society at the Hammond City Hall recently the speakers were Drs. Edgar Burns on urinary infections and Conrad G. Collins, vaginitis; both are of New Orleans.

MARYLAND

Group Instruction in Antepartum Care.—The first unit for group instruction in antepartum care was recently organized in the Southeastern Health District under Dr. John A. Skladovsky, district health officer, and Miss Rae D. Serpick, supervisor of public health nurses. Each Wednesday since the first meeting about twenty-five mothers have met to receive instruction and to witness practical demonstrations of the essential points in antepartum hygiene and infant care. Later it is hoped to establish a similar plan of health education for prospective fathers.

MASSACHUSETTS

Fellowships for Psychoanalytic Training.—The Boston Psychoanalytic Institute announces three Sigmund Freud fellowships in psychoanalytic training to begin in September 1939. The fellowships are open to graduates of class A medical schools who have had at least one year of general hospital training and two years' training in psychiatry. Applications must be filed before Feb. 1, 1939. Further information may be obtained from Dr. Moses Ralph Kaufman, chairman of the educational committee, 82 Marlborough Street, Boston.

MICHIGAN

Graduate Obstetrical Training.—Dr. Sprague H. Gardiner, senior instructor in obstetrics, University of Michigan Medical School, Ann Arbor, has been appointed in charge of a course of graduate instruction in obstetrics and gynecology. He will serve under the direction of Dr. Norman F. Miller, professor and head of the department of obstetrics and gynecology at the university. The course provides for two weeks of intensive training and observation in obstetrics, gynecology and allied subjects at University Hospital. Two practicing physicians are appointed for each period. Appointees for the quarter beginning October 1 include Drs. William G. Winter Jr., Nelson H. Clark, Harry C. Irvin, Holland; Gabriel D. Bos, Marvin B. Meengs, Muskegon Heights; William R. Lyman and George Loupee, Dowagiac; Clayton H. Palmer, Cassopolis; Sabina Kessler-Frux, Bay City, and Oscar D. Stryker, Fremont.

Pneumonia Program.—The Michigan State Department of Health will begin a program this fall to place production of pneumonia serum on the same basis as other biologic products so that state produced serum may eventually be made available to all residents of Michigan. The pneumonia program in Michigan was made possible by a grant of \$50,000 from the Commonwealth Fund to cover experimentation with the production of antipneumococcus serum for three years. The last legislature matched this amount, but the governor reduced it to \$30,000 because of unanticipated needs of relief. Distribution will start this fall, the use of state serum being restricted to the treatment of persons for whom serum is otherwise not available. The only other restrictions are that the determination of type be made by a registered laboratory and that physicians give the department of health a report on cases in which state serum is used. Michigan now has seventy-four typing stations, all but two of which are located below the Bay City-Muskegon line, the other two being in Houghton and Marquette in the Upper Peninsula. Thus far eight serum distributing stations have been established, two in the Upper Peninsula and six in the Lower in Houghton, Marquette, Muskegon, Grand Haven, Grand Rapids, Lansing, Saginaw and Pontiac. Typing facilities are available in thirteen other counties in Lower Michigan and distributing centers will be established in these counties as rapidly as arrangements can be made with the medical societies in these counties. Present facilities will accommodate about one third of the people of the state outside of Wayne County. A subcommittee on pneumonia of the preventive medicine committee of the state medical society agreed to cooperate with the department by giving the program a prominent place on the state medical society's program and by providing speakers for the extension courses carried on throughout the winter jointly by the state medical society and the University of Michigan.

MINNESOTA

Alumni Meeting.—The Minnesota Medical Alumni Association will hold a meeting October 14, the day of the University of Minnesota homecoming football game, at the University Hospitals, Minneapolis, under the chairmanship of Dr. Harold G. Benjamin. Clinics will be conducted in Todd Amphitheater by Drs. Ralph T. Knight in anesthesia; Horace Newhart, otolaryngology; Irvine McQuarrie, pediatrics; Owen H. Wangenstein, surgery; John L. McKelvey, obstetrics; Cecil J. Watson, internal medicine, and John C. McKinley, neurology. In the evening a dinner at the Minnehaha Club will be held in honor of Dr. Jennings C. Litzénberg, retiring head of the department of obstetrics.

MISSISSIPPI

District Meeting.—Dr. George W. Crile, Cleveland, addressed the Northeast Mississippi Thirteen-County Medical Society, Amory, September 20 on "An Analysis of the Indications and End Results of Surgical Treatment in 425 Cases of Essential Hypertension." Dr. J. Rice Williams, Houston, discussed "X-Ray Therapeutics" and Dr. William A. Evans, Aberdeen, "Preventing Pneumonia."

MISSOURI

Lectures on Obstetrics and Pediatrics.—The Missouri State Medical Association is sponsoring a series of lectures throughout the state on obstetrics and pediatrics as a continuation of a program begun in July. The speakers are Drs. Oscar F. Bradford, Columbia, and Paul F. Fletcher, St. Louis, who address lay groups the first four days of a week, on the importance of visiting a physician early in pregnancy, continuing under the physician's care until the baby is born and at least 1 year old. On the afternoon or evening of Friday of each week a meeting of physicians of the counties, sponsored by the medical societies, will be addressed by Dr. Fletcher and Dr. Bradford.

NEW HAMPSHIRE

Blood Test Required for Marriage License.—New Hampshire's law requiring a blood test for syphilis of all persons seeking licenses to marry, enacted in August 1937, became effective October 1. Before a town or city clerk issues a license, he must have in his possession a physician's statement that neither applicant is afflicted with syphilis or if afflicted is not in a stage in which the disease may become communicable. This statement must be accompanied by a record of a standard blood test. The result of the laboratory test is confidential and does not become part of the marriage record. To be acceptable the test must be made at the state laboratory.

of hygiene at Concord. No charge is made for the laboratory service. Out of state applicants must conform to the requirements laid on New Hampshire residents.

NEW JERSEY

State Society Checks Need for Medical Care.—In connection with its survey of the need and supply of medical service, the Medical Society of New Jersey in July invited every person in New Jersey in need of medical care and unable to obtain it to communicate with the society's office in Trenton. The announcement was made through newspapers and radio channels. The society reports that in the first ten weeks 120 requests were received and all were turned over to the medical societies in the counties in which they originated. The requests were promptly investigated and care provided when it was needed. It was found that many requests came from persons who had already had medical care but were dissatisfied for various reasons. Requests came principally from persons who had no funds and did not know how to go about obtaining medical care. The society's report points out that 120 persons who apparently believe themselves unable to obtain medical care is a small proportion out of a state population of more than four million, that care was actually provided for some who did not know how to obtain it, and that newspapers lauded the plan as an effort to make medical care available.

NEW YORK

Cornerstone Laid for New Academy Home.—The Rochester Academy of Medicine held an official ceremony of laying the cornerstone of its new home August 22. A residence, presented to the academy recently by the daughters of the late Edmund Lyon, is being remodeled and a \$60,000 auditorium is being added. Dr. Albert D. Kaiscr, president of the academy in 1937, made the principal address and the present president, Dr. David B. Jewett, presided. Dr. William W. Percy has been named to a newly created position of executive director. His task will be to coordinate the functions of the academy and to supervise the moving into the new building. The former home of the academy has been sold to the University of Rochester.

New York City

Hospital News.—The New York Polyclinic Medical School and Hospital announces the opening of the urologic department in its new clinic building under the supervision of Drs. Joseph F. McCarthy, Daniel A. Sinclair, David Geiringer and Howard S. Jeck and their associates.

Unusual Prevalence of Whooping Cough.—More than 400 cases of whooping cough are being reported weekly to the New York City Department of Health, it was announced September 4. So far this year there have been 8,552 cases with seventy-two deaths. In the corresponding period of 1937 there were 2,646 cases and twenty-nine deaths, it was said.

Meetings of the Academy.—The New York Academy of Medicine announces a change in policy for its stated monthly meetings. To stimulate interest, programs for the coming year have been arranged to provide consideration of controversial issues. In certain instances, according to the *Bulletin*, discussion has been devised to invite conflicting opinions on measures now before the medical profession. The first meeting will be held October 6 and the subject will be "Evaluation of Sulfanilamide Therapy." Dr. Eli K. Marshall Jr., Baltimore, will speak on "Fundamental Problems of Chemistry and Pharmacology—Mechanism of the Action" and Dr. Reuben Ottenberg, "Clinical Aspects." The discussers will be Drs. Francis G. Blake, New Haven, Conn., on erysipelas; Emanuel Appelbaum, meningitis; Hainer F. Swift, rheumatic fever; William E. Studdiford Jr., gonorrheal conditions and postpartum infection.

Attempt to Smuggle Narcotics in Ice Cream.—Three men were arrested as would-be smugglers of narcotics September 20 on evidence showing they had attempted to send 77 grains of heroin to two prisoners who were being questioned in the office of the United States marshal. The men ordered ice cream and sandwiches to be delivered from a restaurant to the two prisoners. When it was prepared the men asked to see the ice cream, and the man at the counter saw the customer put something in the package. When the men had gone the restaurant clerk telephoned the marshal's office, where investigation revealed the capsule of heroin. The three men were already under indictment for conspiracy to violate the narcotic law and were arrested in court after they had pleaded guilty to the first charge. One was sentenced September 23 to eight years in prison on the old indictment; sentence for the other two was deferred. The two men for whom the smuggled heroin was intended were also sentenced on the same old indictments to terms of three and eight years.

NORTH DAKOTA

Special Society Organized.—The North Dakota Society of Obstetrics and Gynecology was recently organized with the following officers: Drs. James F. Hanna, Fargo, president; John H. Moore, Grand Forks, vice president, and August C. Orr, Bismarck, secretary.

OHIO

Regional Annual Meeting.—The ninety-fourth annual meeting of the Northwestern Ohio Medical Association will be held in Defiance October 4 under the presidency of Dr. Edward B. Pedlow, Lima. Among the speakers will be:

- Dr. Harold N. Cole, Cleveland, Precancerous Dermatoses and Malignancy of the Skin.
- Dr. Robert L. Schaefer, Detroit, Clinical Indications for the Anterior Pituitary-like Hormone.
- Dr. William Halsey Barker, Baltimore, Sulfanilamide.
- Dr. Henry W. Meyerding, Rochester, Minn., Displacement of the Lumbosacral Spine Associated with Backache.
- Dr. Emil Novak, Baltimore, Endocrine Aspects of Sterility.

The meeting will be preceded by a golf tournament Monday afternoon October 3.

OKLAHOMA

Courses in Venereal Disease.—With funds appropriated under the LaFollett-Bulwinkle bill, a series of lectures for physicians on venereal disease will begin October 3 in four counties to run for five weeks. The lectures will be given Mondays at Claremore, Rogers County; Tuesdays at Pawhuska, Osage County; Wednesdays at Bartlesville, Washington County, and Thursdays at Vinita, Craig County. Dr. David V. Hudson, Tulsa, will be the lecturer.

OREGON

Gift to University Medical School.—A gift of funds has been made to the University of Oregon Medical School, Portland, by Mrs. Julius L. Meier and her family in memory of the late Gov. Julius L. Meier. The initial gift amounts to \$50,000, it is announced, and will be added to funds for construction of the new University State Tuberculosis Hospital to be built on the university grounds. The legislature appropriated \$110,000 and the PWA allotted \$90,000 for the hospital; the added \$50,000 will make possible construction of forty beds in addition to the thirty-nine originally planned, Dr. Richard B. Dillchunt, dean of the medical school, announced. It will also make possible better outpatient facilities, it was said.

PENNSYLVANIA

Expand State Tuberculosis Facilities.—A new surgical unit at the State Sanatorium for Tuberculosis, Hamburg, was dedicated July 7 by Dr. Edith MacBride-Dexter, state secretary of health. Cornerstones were laid August 18 by Dr. MacBride-Dexter for a main infirmary, a children's preventorium and a dormitory for women employees at Pennsylvania State Tuberculosis Sanatorium, South Mountain.

District Meeting.—Dr. Martin E. Rehffuss, Philadelphia, addressed a meeting of the Second Council District, Medical Society of the State of Pennsylvania, Norristown, September 15, on "Gastric Neuroses." Dr. Frederick J. Bishop, Scranton, president of the state society, spoke on "The Status Quo of Medicine" and other state officers discussed current problems. Testimonials were presented to the following physicians who have been in practice fifty years: Drs. John L. Bower, Birdsboro; William T. Sharpless, West Chester; U. Grant Gifford, Kennett Square, and Nathaniel C. Peters, Northampton.

Philadelphia

Refresher Course for Nurses.—The Philadelphia General Hospital will offer a special four weeks refresher course to graduates of its school of nursing beginning October 1. One week will be spent in each of the major services (medicine, obstetrics, surgery and pediatrics), with experience in various special departments. The course will be repeated in January, April and June 1939. Graduates of the hospital who wish to take the course may communicate directly with the Director of Nursing, Miss Loretta M. Johnson, at the hospital.

UTAH

State Medical Election.—Dr. George M. Fister, Ogden, was named president-elect of the Utah State Medical Association at its annual meeting in Ogden September 1-3 and Dr. Claude L. Shields, Salt Lake City, was installed as president. Vice presidents elected were Drs. George L. Rees, Smithfield; Harry S. Scott, Salt Lake City, and Bliss L.

Finlayson, Price. The next annual meeting will be in conjunction with the Rocky Mountain Medical Conference in Salt Lake City, September 5-7, 1939.

VIRGINIA

Changes in Health Departments.—Rockbridge County has recently been separated from the Alleghany-Botetourt-Rockbridge health district to form a unit with the city of Lexington, with Dr. Robert P. Cooke continuing as health officer. Dr. James H. Gordon, Covington, has been appointed health officer of the new district of Alleghany and Botetourt counties. Dr. William Y. Garrett, Raven, has succeeded Dr. James N. Dudley, Eastville, as health officer of Northampton County. Dr. Charles H. Bondurant, Wytheville, has been made health officer of Wythe County and Dr. Eugene Bowie Shepherd, Baltimore, assistant health officer of Pittsylvania County.

WISCONSIN

Lectures on Infectious Diseases.—A series of lectures on infectious diseases will be presented by the committee on postgraduate education of the Medical Society of Milwaukee County with the following speakers: Drs. Henry C. Sweany, Chicago, on "Pulmonary Tuberculosis," October 10; John A. Kolmer, Philadelphia, "Value of Serums and Vaccine in General Medicine," October 18, and Joseph Brennemann, Chicago, "Contagious Diseases of Childhood," November 1.

WYOMING

State Medical Election.—Dr. John H. Goodnough, Rock Springs, was named president-elect of the Wyoming State Medical Society at its annual meeting in Laramie August 7-9 and Dr. John D. Shingle, Cheyenne, was installed as president. Dr. Marshall C. Keith, Casper, is secretary. The 1939 meeting will be held in conjunction with the Rocky Mountain Medical Conference in Salt Lake City, September 5-7.

GENERAL

Rocky Mountain Tuberculosis Conference.—The fourth biennial meeting of the Rocky Mountain Tuberculosis Conference will be held October 7-8 in Salt Lake City at the Hotel Utah. Twelve Rocky Mountain states make up the conference, of which Dr. Harry J. Corper, Denver, is president. Among the speakers will be:

- Drs. John Zarit and Allen D. Riemer, Denver, Colo., Syphilis of the Lung.
- Dr. Edward E. H. Munro, Grand Junction, Colo., Silicosis.
- Dr. Leslie P. Anderson, Elma, Wash., Development of Allergy in Relation to Tuberculous Lesions in Young Adults.
- Dr. Charles J. Kaufman, Denver, Vocational Therapy in the Management of Pulmonary Tuberculosis.
- Dr. Kendall Emerson, New York, The Philosophy of the National Tuberculosis Association on Rehabilitation and After-Care.
- Dr. Walter I. Werner, Albuquerque, N. M., Tuberculous Trachetitis.

At a banquet Friday evening Dr. Corper will deliver his presidential address on "Neo-Hippocratic Tuberculosis" and Dr. James J. Waring, professor of medicine, University of Colorado School of Medicine, Denver, will be the guest speaker on "Prognosis in Tuberculosis."

National Safety Congress in Chicago.—The Silver Jubilee meeting of the National Safety Congress will be held in Chicago October 10-14 at the Stevens Hotel. Addresses of medical interest include the following:

- W. C. James, safety engineer, Portland Cement Association, Chicago, What About the Health of Quarry Workers?
- Dr. Morris Fishbein, Chicago, Editor of THE JOURNAL, Personal Hygiene and Its Relation to Syphilis Control in the Food Industry.
- Dr. Albert E. Russell, U. S. Public Health Service, Washington, D. C., Industry's Part in Combating Venereal Diseases.
- Dr. Harold A. Vonachen, Peoria, Ill., What Can Be Done About Fatigue?
- Dr. Harry E. Mock, Chicago, A Surgeon's Experience with Industrial Injuries.
- Dr. Edward C. Holmlund, Chicago, Problems in the First Aid Treatment of Fractures.
- Dr. Carey P. McCord, Detroit, Handicaps in the Diagnosis of Occupational Diseases.
- Dr. Milton H. Kronenberg, Chicago, The Necessity for Uniform Absenteeism Records in the Industrial Health Program.
- Dr. John J. Wittmer, New York, Has the Public Utilities Industry Any Occupational Health Hazards?

At the silver jubilee banquet Wednesday evening October 12 the speaker will be George E. Vincent, Ph.D., former president of the Rockefeller Foundation, New York.

Examinations in Obstetrics and Gynecology.—The American Board of Obstetrics and Gynecology announces that examinations for Group B candidates will be held in various cities of the United States and Canada Nov. 5, 1938, and Feb. 4, 1939. Application for the written examination for February must be filed with the secretary of the board before December 4. The general oral, clinical and pathologic examinations

for all candidates (groups A and B) will be conducted by the entire board, meeting in St. Louis May 15-16, 1939, during the week of the annual session of the American Medical Association. Applications for the group A examinations must be filed with the secretary before April 1, 1939. For further information and application blanks address the secretary, Dr. Paul Titus, 1015 Highland Building, Pittsburgh.

Central Association of Obstetricians and Gynecologists.—The tenth annual meeting of the Central Association of Obstetricians and Gynecologists will be held at the Hotel Radisson, Minneapolis, October 6-8, under the presidency of Dr. Robert D. Mussey, Rochester, Minn. Dr. Jennings C. Litzenberg, who recently retired as professor of obstetrics and gynecology at the University of Minnesota Medical School, Minneapolis, will be the guest of honor and will deliver an address entitled "The Making of a Conservative." Among the speakers will be:

- Drs. Percy B. Russell Jr., and Michael J. Roach, Memphis, Tenn., B. Welchii Infections in Pregnancy.
- Drs. Robert Jerome Prentiss and Warren W. Tucker, Iowa City, Cystography in the Diagnosis of Placenta Praevia.
- Drs. Ralph A. Reis and Melvin B. Sinykin, Chicago, Myomectomy During Pregnancy.
- Dr. Philip F. Schneider, Evanston, Ill., Prophylactic Endocrine Therapy in Surgical Menopause.
- Dr. John Milton Singleton, Kansas City, Mo., The Effect of Alkaline Vaginal Preparations on the Huhner Test and Sterility.

A symposium on "Some Aspects of the Vascular Changes in Pregnancy Toxemias" is to be presented by the following members of the faculty of the University of Minnesota Medical School: Drs. Litzenberg, Maurice B. Visscher, Elexious T. Bell and John L. McKelvey. A banquet will be held Friday evening at which winners of the annual prize awards will present their papers. They are Drs. Fred L. Adair and John A. Haugen, Chicago, on "A Study of Suspended Human Muscle Strips in Vitro" and Drs. Ward F. Seeley, Roger S. Siddall and Walter J. Balzer, Detroit, on "Collapse Therapy for Tuberculosis in Pregnancy." At the banquet Dr. Mussey will deliver his presidential address on "Pelvic Pain" and Dr. Everett D. Plass, Iowa City, will speak on "The Birth of an Influence."

Government Services

Examinations for Army Medical Corps

The War Department announces an examination December 5-9, both dates inclusive, for qualification of candidates for appointment as first lieutenants in the U. S. Army Medical Corps to fill vacancies during the fiscal year 1939. The examination is open to all male graduates of acceptable medical schools who have completed one year's internship in an approved hospital and who will not be over 32 years of age at the time it will be possible to tender a commission. Boards of medical officers will convene throughout the United States to conduct the examination, which will consist of a physical examination, a written examination in professional subjects and a determination of the candidates' adaptability for military service. Licentiatees of the National Board of Medical Examiners may be exempted from the written professional examination. Full information and application blanks will be furnished on request to the Adjutant General, War Department, Washington, D. C. Applications must be filed by November 19.

Public Health Service to Investigate Pneumonia

Field research projects in cooperation with state and local health departments have been established by the U. S. Public Health Service in seven states for an intensive investigation of the treatment and spread of pneumonia. Studies will be made in New Jersey, Pennsylvania, Illinois, St. Louis, Denver, New Orleans and a selected north central area in California. Three aspects will be covered: incidence of pneumonia by type, effectiveness of different serums in reducing pneumonia mortality and effectiveness of certain chemical substances in treatment. Funds will come from the regular scientific appropriation of the public health service, funds appropriated for public health purposes under the Social Security Act and state and municipal health budgets. Actual direction of the projects will be in the hands of the state or local health officers; the federal health service will lend technical assistance, act as consultant and in cooperation with local authorities tabulate and synthesize the results for publication. Public health service officers in charge of the studies are Drs. Joseph W. Mountin, Adolph S. Rumreich and Claude D. Head Jr.

Foreign Letters

LONDON

(From Our Regular Correspondent)

Sept. 10, 1938.

"The Doctor's View of War"

The medical profession plays an active part in war, and the question What should be its attitude toward war is discussed in a small book, "The Doctor's View of War," edited by Dr. Horace Joules and written by nine physicians with the collaboration of a score of others. In a foreword Prof. J. A. Ryle says that our profession may be claimed to be the only pacifist one in the world. Yet the physician has become a partner in modern war, for he pronounces men fit for service, inoculates them against infections, supervises their health and patches them up again for the ordeal of battle. Professor Ryle remarks that it is an arresting, if at present fantastic, thought that our profession, which is more international than any other, could, if well coordinated, of its own initiative put a stop to war or at least so hamper the most bellicose government as to give it pause. Internationalism, he thinks, will eventually pave the way to peace. The great war occurred after a period of remarkable advance in medical science and on the western front was free from the usual outbreaks of infectious diseases, although new diseases appeared and there was a large incidence of minor infections. In the East the old enemies dysentery, typhus and malaria were endemic. War neuroses do not differ essentially from those of peace but because the precipitating factors are more violent they are more striking. In the great war the neuroses were clinically in two groups, officially called neurasthenia and hysteria. Those in the former group would now be called anxiety neuroses. An example of the injustice of war was that it was the merest accident, sometimes depending on the whim of a superior officer, whether a man was labeled "shell shocked" and sent to the hospital or had to face a court martial and firing squad for cowardice.

Some persons extol war as "nature's pruning hook," but the only biologic advantage it has is hybridization, of which they do not appear to be aware. This has made possible new and more and more favorable combinations of characteristics, but there is no reason for thinking that modern warfare has any eugenic value comparable to its destructiveness. There are no signs of biologic significance attaching to the great war; both victors and vanquished have the same menace of a rapidly falling population. If there is a selective effect within a national group it is probably dysgenic. The most optimistic view is that modern war will wreck the structure of society without inflicting any permanent biologic damage.

A deplorable practice in recent wars is disregard of the Red Cross. Hospital ships were sunk in the great war, and an attack on a Canadian hospital at Doullens is well authenticated. In Abyssinia the Red Cross was systematically bombed, and in the hospital at Dessie an American nurse was wounded and patients and their attendants were killed. Disregard of the Red Cross and bombing of cities is seen in the wars in Spain and China. The authors suggest that we appear to be on the verge of another age of barbarism. The hope lies in the stubborn democratic spirit of certain countries, which refuses to be intimidated by the philosophers of war absolute.

What can the medical profession do to avert this great calamity? After advocating strengthening of the League mechanism for collective security, the authors suggest that the medical association of one of the great civilized and democratic countries should take the lead by summoning the medical societies of all other countries to a conference, which should issue a pronouncement declaring it to be the will of the profession that for the sake of humanity a system of collective security should be established.

A Nurse Is a "Workman"

Under the workmen's compensation act a person is entitled to compensation for an accident arising in or out of his employment, but this has sometimes given rise to the question What constitutes employment? Are professional footballers or film stars employed in the legal sense? A decision of considerable importance to hospitals has been given in the case of a nurse who, acting under the directions of a ward sister in a municipal hospital, was preparing a poultice which exploded in the can in which it was being heated and injured her. She applied in court for compensation, but the judge held that she was not acting under a contract of service but under a contract to perform a service as an independent expert. The case was taken to the court of appeal. An argument took place as to whether a distinction could be drawn, as in a previous case, between the skilled technical duties of a nurse and her administrative or ministerial duties (which constituted employment without any doubt). One judge thought that it could and that when she was doing her work as a nurse the hospital was not liable to pay damages for her negligence or to compensate her. But the two other judges disagreed, and so she won her case. One said that her contract of service could not be divided and that, although the hospital might choose the person whom she was called on to obey, she was always under obedience to the hospital. The other judge said that negligence cases could not be applied to the question at issue. So manifestly were nurses in the service of their hospital that for this very reason it was necessary in a negligence case to inquire whether the hospital was liable for their negligence. The nurse was the servant of the hospital for general purposes and was under a contract of service with it under the workmen's compensation acts. The case was therefore sent back to the lower court for the judge to assess the compensation payable. The hospital was given leave to appeal to the highest court, the House of Lords.

Sir David Wilkie

The Edinburgh medical school has sustained a great loss by the death, at the age of 56, of Sir David Wilkie, professor of surgery. Born in Kirriemuir, the "Thrums" of the novelist J. M. Barrie, who was an intimate friend, he was educated at the University of Edinburgh, from which he graduated in 1904. In 1909 he took the Ch.M. degree and received a gold medal for his thesis. He became a fellow of the Royal College of Surgeons of Edinburgh in 1907 and of the similar college of England in 1918 and was made an honorary fellow of the American College of Surgeons in 1926. He was not only a great surgeon and a great teacher but an active member of many scientific boards, such as the Medical Research Council and the Scientific Advisory Committee of the British Empire Cancer Campaign, and was president of the section of surgery at the Edinburgh meeting of the British Medical Association in 1927.

The conservative treatment of acute infections was perhaps the most important part of his impressive teaching. The operative zeal which naturally followed Lister's great discovery was followed today, he said, by a fundamental change, as surgeons thought more on biologic and less on mechanical lines. The delicate and complex series of local and general changes which were the reaction to local infection had as their main objects localization of the infection and mobilization of the body forces. Nothing should be done which interfered with this process. At the recent annual meeting of the British Medical Association he opened the discussion on septic hand. He held that the profession had not sufficiently recognized the value of Bier's treatment. If the infection could be localized for only a short while, time was gained for general defense. His method was to apply the thin elastic bandage very lightly to the upper arm and leave it on for not less than twenty-two of the twenty-four hours, preferably continuously, for three days. If the bandage was applied correctly there would be no dusiness of the limb, only slight swelling, and the pain would be relieved. Incision of a

boil on the supposition that it is a form of abscess he held to be wrong in theory and mischievous in practice. Complete immobilization by strapping was the best treatment, and this held also for carbuncle, though in cases of severe toxic involvement antitoxic serum should be given. Experiments on rabbits convinced him that there was no active surgical treatment for general peritonitis. It might be prevented by timely surgical intervention and complications might require surgical aid, but confidence must be placed in medical remedies, serums, fluid replacement for vomiting, heat and morphine. Empyema he treated by aspiration, saying that the appalling death rate in the American army following open drainage of streptococcal empyema was necessary to bring home this lesson.

PARIS

(From Our Regular Correspondent)

Sept. 3, 1938.

Use of Refrigerated Blood for Armies

The war clouds hanging over European countries have given an impetus to the study of whether refrigerated, or conserved, blood can be used on a large scale at or near the front. The employment of such blood during the present civil war in Spain has shown that it is an important addition to the resources of the military surgeon. At the June 29 meeting of the Académie de chirurgie of Paris, the head of a large army hospital, Dr. Maissonnet, and Professor Jeanneney of Bordeaux, who has been one of the most enthusiastic advocates in France of the use of refrigerated blood, read a paper on the organization of a service to supply such blood during war. Extensive studies have shown that blood which has been kept at a temperature of 4 C. retains all its therapeutic qualities for from ten to fifteen days. The red blood cells, although they do not decrease in number, show slight morphologic changes such as contraction, a dentated appearance and expulsion of a part of the hemoglobin, and at the end of twenty days hemolysis can be noted. The leukocytes appear to undergo destruction as the result of refrigeration. From the chemical point of view, the blood gradually loses its dextrose content, but the phosphorus and the protein content increase, probably as the result of lysis of the leukocytes. As to the physical properties of the blood, especially its density and electrical conductivity, these show changes from the twelfth day onward. The biologic properties of the blood remain practically the same, especially as to grouping. The respiratory capacity does not show any alteration until about the twentieth day. These observations show that refrigerated blood, at least during the first week, resembles so closely fresh blood as to make it safe to use the former as a substitute. The authors cited the use of refrigerated blood during the civil war in Spain. A transfusion center was organized at Barcelona in 1936, the donors being nonmobilized civilians, especially women. From each of the 4,500 donors about 400 cc. was taken every month or so. During the first year 1,220 liters of blood was thus made available to be sent to the front either by trucks or by special automobiles equipped with electrical refrigerators similar to those in domestic use. On the insurgent side twenty transfusion centers were organized. Over 9,000 persons from 16 to 50 years of age served as voluntary donors, some of them more than twelve times. Every brigade has its transfusion service, and the blood can be given at the front by using boxes constructed on the principle of a vacuum bottle so as to keep it at the same temperature as in a refrigerator. The government surgeons use a citrated blood, whereas in the insurgent armies the whole blood method as advocated by Yudin of Moscow (described in an editorial in *THE JOURNAL* August 20) is employed. The results, as published in recent bulletins from both armies, have been equally satisfactory.

Maissonnet and Jeanneney are of the opinion that refrigerated blood will render valuable service in future wars. Their experi-

ence in its use in peace times is limited to citrated blood. A French military surgeon, Pilod, in 1936 offered a plan for the organization of a transfusion or hematologic service for each division consisting of a chief and three aids who are specialists in the examination of donors and recipients as well as in giving transfusions. It should be the duty of such teams to obtain blood from slightly wounded or convalescent soldiers and to keep on hand a relatively large amount of blood of different groups. First aid and casualty clearing stations would thus be provided with flasks containing 250 cc. of blood from universal donors, which can be given intravenously by any surgeon. It would rarely be necessary to obtain blood from the personnel of the hospital corps. In addition to this service at or near the front, a service would be organized in every region of the country which would have as its objective the collection of a reserve supply from civilian donors, including blood from all four groups. This blood could be sent to the front by means of airplanes or automobiles equipped with apparatus to keep the blood at a low temperature. Professor Jeanneney, so that automobiles with refrigeration facilities can be dispensed with, is studying the use of a specially constructed box to contain a large number of flasks of conserved blood which can be kept at a temperature near 4 C. and can therefore be transported by ordinary army trucks. The blood can then be warmed before being used for transfusion.

Program of Therapeutic Union Meeting

This year's meeting of the Therapeutic Union will be held on October 12 at the Paris Medical School. The president is Prof. Maurice Loeper, and reports on the following subjects will be read: oxygen therapy, protein therapy of diabetes, vitamin therapy of diseases of the digestive apparatus, chlorophyll and cutaneous diseases, and continuous intravenous injection as a therapeutic method. A series of papers will be read on the part of sulfur in therapeutics. Information regarding the meeting may be obtained by writing to Dr. G. Leven, 24 rue de Téhéran, Paris 8.

French Syphilology and Dermatology Congress

This year's Syphilology and Dermatology Congress will be held in Paris October 12-14. The president is Dr. Milian, and the program includes reports on balanoposthitis by Dr. Bory, Professor Farre and Dr. Golay; on histamine in dermatosyphilology by Drs. Weissenbach and Jausson and Dr. Kitchevatz of Yugoslavia, and on agranulocytosis in dermatovenereology by Dr. Touraine, Professor Watrin, and Professor Marin of Montreal.

BERLIN

(From Our Regular Correspondent)

Aug. 22, 1938.

Hospitals in the German Reich in 1936

A comprehensive statistical report for the year 1936 on hospitals of the German Reich has just been published. The total number of hospitals was 4,792 as against 4,864 in the year 1935. Of the total number 2,106 were classed as public, 1,552 as communal and 1,134 as private. The smaller number as against the year 1935 was due to the discontinuation of most of the smaller units, namely those having twenty-five beds and less. On the other hand, the number of regularly available hospital beds in the entire country had somewhat increased; it was 620,751 as against 614,888 in 1935. Accordingly there were available an average of 92.2 regular sick beds per 10,000 of population as against ninety-two in 1935.

The number of beds available in various classes of institutions enumerated in 1936 are set forth in table 1.

The gross number of patients treated in the nation's hospitals was 3.7 per cent higher than in 1935. The distribution of patients according to sex is shown in table 2.

As a consequence of the increased number of admissions the number of sick days spent in hospital increased by about 2.8 per

cent, reaching 180,552,492. Accordingly, despite the further decline in the average per patient stay in hospital, which sank from 35.2 to 34.9 days, the utilization of beds was extraordinarily greater, reaching nearly 80 per cent of capacity.

According to season the highest average patient population fell in November; the next highest averages were in February and March. The fewest admissions took place in April.

TABLE 1.—Beds Available in 1936

Classification	Number	Beds
General hospitals	3,196	338,683
Hospitals for tuberculous adults	187	24,319
Hospitals for tuberculous children	31	4,841
Nursling and children's hospitals	154	14,601
Orthopedic hospitals	47	9,080
Eye hospitals	102	3,153
Hospitals for treatment of venereal diseases and dermatoses	36	2,833
Hospitals for chronic invalids and incurable patients	117	19,536
Hospitals and sanatoriums for mental diseases	260	154,032
Institutions for the feeble-minded	64	23,670
Hospitals for nervous disorders	52	2,977
Hospitals for alcoholic and other addicts	18	807
Lying-in hospitals	204	9,358
Other specializing institutions	225	9,513
Hospital units in penal institutions	99	3,348

The gross number of deaths in all German hospitals is shown in table 3.

Although the mortality during the years from 1932 to 1934 remained at the same level, 4.7 per hundred patients, the rate rose to 4.8 in 1935 and to 4.9 in 1936. The influenza epidemics may be presumed to have played a part in this increase. Other possible factors are the increase in serious accidents following the revival of industry and the increasing tendency in recent years to hospitalize seriously ill patients a short time prior to death. Attention was recently called to the latter trend by the municipal medical councilor of Berlin (*THE JOURNAL*, April 30, 1938, p. 1501). Of 100 deaths within the German reich during 1936, 31.9 occurred in hospitals as against only 26.7 in the year 1932.

Table 4 illustrates the distribution of various types of obstetric cases.

TABLE 2.—Distribution of Patients by Sex

Year	Total	Male	Female
1935	4,994,000	2,352,000	2,642,000
1936	5,177,000	2,449,000	2,728,000

TABLE 3.—Number of Deaths

Year	Total Persons Dying in Hospital	Male	Female
1934	215,561	112,687	102,874
1935	241,883	125,874	116,009
1936	254,127	133,735	120,392

The number of completed confinements in all hospitals increased by about 6.8 per cent as against the year 1935. On the other hand, the number of artificial interruptions of pregnancy performed in hospitals declined by about 28 per cent, apparently as a result of stricter control of the necessitating circumstances.

Particularly important to the national eugenic health policy is the determination of the proportion of institutional births to the total number. In 1936 1,312,053 babies were born in Germany; the per mille proportion of babies born in hospitals was 269.9 as against 251.2 in 1935. The number of institutional births has accordingly undergone not only an absolute increase

but an increase in proportion to the total number of births. The birth rates of certain localities have declined considerably as a result of increased hospitalization in confinement cases.

In the report under discussion, data on the hospitals of Austria are submitted for the first time since the country was annexed. In the year 1936, 287 hospitals were enumerated, fifteen of them institutions for the insane. There were ninety-six public hospitals with a total of 36,505 beds; 12,366 beds, namely one third of the total, were in hospitals for the insane. There were 191 nonpublic hospitals with a total of 15,682 beds; included in this group were five small hospitals for the insane with 553 beds and forty-seven sanatoriums with 2,679 beds. The total number of beds available in Austrian hospitals was accordingly 52,187 (77.8 per 10,000 of population); the bed capacity was thus smaller by some 14.4 per 10,000 than that of the German reich.

The supply of hospital beds differed widely in the various provinces of the Austrian federation. In Vienna, for example, there were 95.6 beds per 10,000 of population; for Burgenland, on the contrary, the corresponding figure was only 14.4.

The total number of persons hospitalized in Austria in 1936 was 583,171, of whom 21,080 were treated in hospitals for the insane. The total number of days in hospital was 16,051,928, of which 5,026,434 represented days spent in hospitals for the insane. The average stay in hospital was 27.6 days. The beds utilized represented 84 per cent of capacity, a somewhat larger proportion than in the German reich. During the year 23,937

TABLE 4.—Distribution of Obstetric Cases

Confinements	Total Number	In Lying-in Hospitals and Services	Percentage
1935	321,310	248,638	77.4
1936	349,092	264,809	75.9
Induced Abortions			
1935	4,151	1,905	45.9
1936	2,982	1,301	43.6
Miscarriages			
1935	87,182	33,422	38.3
1936	88,667	35,817	40.4

persons died in hospitals, namely 4.1 per cent of the patient population and 26.9 per cent of all persons dying in Austria in 1936.

Dosage of Ultraviolet Radiation

Dr. Wucherpfennig's fundamental discussion of the dosage of ultraviolet radiation before the medical society of Münster, Westphalia, was based in part on his own investigation. Even if the practitioner has at his disposal a dosimeter for ultraviolet rays he is still in no position to evaluate accurately the biologic reaction of predilection in the individual case. It is assumed that the dosimeter will register precisely the most important biologic reaction, namely the erythema. The erythema, however, as has been demonstrated by the author and others, is peculiarly dependent on the sex and age of the patient and the nature of the disorder. Then too, erythema varies in character according to the region of the body irradiated. Difficulties which cannot be excluded from administration of even the most optimal physical dose may, however, be abolished if the operator gauges his therapeutic procedure by the erythema itself or, as Wucherpfennig calls it, the "erythematous threshold." For practical purposes one may consider this erythematous threshold of the ultraviolet current to be the weakest degree of reddening which is sharply defined against the adjacent unirradiated region within twenty-four hours after irradiation. The roentgen therapy then consists of some ten additional doses of radiation, administered at intervals of one week. Each dose must be about 30 per cent more powerful than the preceding one. This holds true for all ultraviolet current apparatus. The apparatus, for example the mercury quartz lamp and almost all carbon arc lamps with metallic salt carbons, usually emits

a short wave, erythema-producing, ultraviolet ray (an ultraviolet concentration of from 2,800 to 2,400 angstroms). Recent studies of the intermediary metabolism have demonstrated impressively the importance of the mentioned variations up to the average ultraviolet reaction. The investigations, although seemingly of only theoretical worth, have throughout a practical value as well. Cutaneous reactions to the ultraviolet rays produce, according to the degree of their intensity, metabolic processes which may be wholly disparate in character.

BELGIUM

(From Our Regular Correspondent)

Aug. 20, 1938.

The Order of Physicians Established by Law

The Chamber of Representatives has passed legislation establishing an Order of Physicians. This marks a red letter day in the history of the Belgian medical profession. Although for this body the new enactment represents the fruit of tentative negotiations which have been in progress for over a century, it may be said that the question has entered a phase of imminent realization only since 1924. In that year the Académie royale de médecine formally advocated the establishment of an official order of physicians. In recent years we have noted the successive steps in the evolution of this great reform, the social importance of which is well recognized. It seems appropriate to quote the memorable words of the minister Jaspas with regard to this problem: "When an important group such as the medical profession concerns itself with problems of deontology, morale, dignity and honor, it is a matter of interest not only to physicians. The new order of physicians, besides serving as a vital factor in the perpetuation of an organized medical profession, will serve as a strong bulwark to society as a whole." The new statute constitutes a veritable magna carta of Belgian medicine. Its more important provisions are as follows:

The Order of Physicians comprises all doctors of medicine, surgery and obstetrics resident and authorized to practice in Belgium whose names appear in the order's official register. Transitional regulations provide that all doctors of medicine, surgery and obstetrics resident in Belgium who wish to practice in this country must first have themselves enrolled on the order's official register. A provincial council of the order, having local jurisdiction over a particular practitioner, cannot refuse to enroll him unless he has been convicted of some act serious enough to warrant permanent exclusion from the practice of medicine in Belgium.

A physician barred from practice can demand and receive a personal hearing before the council of the order. He may be represented by one or several advocates. The council of the order will explain the motivation of its judgments as rendered.

There is created in each province a council of the order, having jurisdiction over all physicians resident in the province. The councils of the order are charged with upholding the standards of medical deontology, honor, propriety and dignity in their respective memberships. The councils also take cognizance, as competent authorities, of any instances of malpractice allegedly committed within the respective jurisdictions. The councils are empowered to regulate the scale and amount of professional fees in certain cases, namely (1) if serious lack of professional ethics is imputed, (2) on the joint request of two interested parties and (3) in compliance with a judicial request for expert opinion. No physician can be made liable to punishment on religious, philosophical, political, linguistic or syndical grounds or because of his affiliation with an organization concerned with practice of medicine among a particular group or class of persons. Any interference in the foregoing domains is forbidden.

Each council of the order is composed of active members and alternate members elected by the physicians whose names appear in the official list. The number of active and alternate members to be elected is fixed by the royal decree embodied in article 23. Each of the juridical arrondissements of a province shall have at least three representatives on the council. Election of members is by secret ballot. The right of voting is limited to two thirds of the seats provided for each arrondissement. The members of the council of the order, both active and alternate, are elected from among practitioners of Belgian nationality not under 35 years of age who are residents of the particular province and whose names have appeared for at least five years on the official lists of the order. The term of office is four years; members cannot be reelected to succeed themselves. Any member of a duly organized council of the order who absents himself without legitimate excuse from attendance at two consecutive meetings may be punished by admonition or by censure. The officers of a council of the order are elected from its membership; they are the president, vice president and secretary. Each council of the order is assisted in an advisory capacity by a magistrate of first instance appointed by the king. The king also appoints an alternate magistrate under the same conditions.

The superior council of the order of physicians is elected by members of the provincial councils of the order. To complete the membership of the superior council the king appoints one active and one alternate delegate from the faculties of medicine of the universities of Brussels, Ghent, Liège and Louvain. The four universities may submit to the king a list of at least three names. The superior council of the order has its seat at Brussels. It is the duty of the superior council to provide reasoned opinions on questions of general interest; among other things it collects the decisions of various councils with a view to establishment of a body of deontologic jurisprudence. The superior council is to initiate any measures necessary for the accomplishment of its objectives. If the legality of a final decision of the superior council is questioned it may be appealed to the court of cassation. If the latter tribunal finds that a decision has violated the spirit or letter of the statute the decision is set aside. The procedure of appeal to the court of cassation, with regard to both the wording and the time allowed, follows the usual conduct of civil cases. The attorney general may petition the court of cassation for review of a decision of questionable legality. Appeal to the high court is suspensive.

Marriages

WILLIAM HAPPER, London, England, to DR. GLADYS MORGAN of Guntur, Madras Presidency, India, August 15.

WALTER H. SIMMONS JR., Pine Bluff, Ark., to Miss Ruth Wackerman in Norfolk, Va., June 18.

ROBERT LATEINER, New Rochelle, N. Y., to Miss Dorothy Kasenetz of Mount Vernon, July 6.

FRANCIS N. NIMZ, Milwaukee, to Miss Marion Phillips of Stevens Point, Wis., June 28.

WALTER S. POLACHEK, Milwaukee, to Miss Shirley Witkowsky of Chicago, June 1.

OLIVER L. PUTTLER, Milwaukee, to Miss Bergliot Hefte of Staples, Minn., June 25.

JAMES H. GRESSETTE, St. Matthews, S. C., to Miss Mary Sims recently.

CLIFFORD R. SCHNEIDER, Milwaukee, to Miss Eunice Druse, June 25.

GEORGE LIBERMAN to Miss Pearl Cooper, both of Brooklyn, June 11.

DWIGHT MARTIN to Miss Evelyn Kienitz, both of St. Paul, recently.

BERNARD R. BONNOT, Canton, Ohio, to Miss Betty Mang, June 9.

Deaths

Clifford Clarence Robinson * East Chicago, Ind.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1902; fellow of the American College of Surgeons; at one time member of the board of managers of the Lake County Tuberculosis Sanatorium, Crown Point; surgeon to St. Catherine's Hospital, East Chicago, St. Mary's Hospital and Mercy Hospital, Gary, and St. Margaret's Hospital, Hammond; aged 57; died, July 12, in the Augustana Hospital, Chicago, of cerebral hemorrhage and pyelitis.

Melvin M. Franklin, Philadelphia; University of Pennsylvania Department of Medicine, Philadelphia, 1895; member of the Medical Society of the State of Pennsylvania; fellow of the American College of Surgeons; served during the World War; on the staffs of St. Joseph's Hospital, St. Mary's Hospital, Mercy Hospital and the Jewish Hospital and the Veterans Administration; aged 63; died, July 31, at Point Pleasant, N. J., of coronary occlusion.

William Henry Tefft * Colonel, U. S. Army, retired, San Antonio, Texas; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1898; entered the army as an assistant surgeon in 1903; was awarded the Distinguished Service Medal for services during the World War; rose through the various grades to that of colonel; retired March 31, 1937; aged 65; died, July 1, at Fort Sam Houston, of carcinoma of the pancreas.

Edwin A. Hamilton * Columbus, Ohio; Medical College of Ohio, Cincinnati, 1891; assistant professor of surgery, Ohio State University College of Medicine; fellow of the American College of Surgeons; past president of the Columbus Academy of Medicine; served during the World War; on the staffs of the White Cross Hospital and the University Hospital; aged 72; died, July 31, of arteriosclerosis and cerebral hemorrhage.

Samuel Walthall Budd * Richmond, Va.; Johns Hopkins University School of Medicine, Baltimore, 1909; formerly associate professor of pathology and embryology at the Medical College of Virginia; member of the American Society of Clinical Pathologists; on the staffs of the Retreat for the Sick, and St. Luke's Hospital, Richmond, and the Petersburg (Va.) Hospital; aged 55; died, July 27, of heart disease.

Charles Emeric Kerr Vidal, Troy, Mont.; University of Toronto Faculty of Medicine, Toronto, Ont., Canada, 1890, and University of Bishop College Faculty of Medicine, Montreal, Que., 1890; member and past president of the Medical Association of Montana; served during the World War; at one time superintendent of the Montana State Tuberculosis Sanitarium, Galen; aged 68; died, June 20.

Rudolph Rix, Omaha; John A. Creighton Medical College, Omaha, 1899; member of the Nebraska State Medical Association; formerly professor of gynecology and clinical gynecology at his alma mater; past president of the Omaha-Douglas County Medical Society; on the staffs of the Evangelical Covenant Hospital and the Douglas County Hospital; aged 67; died, July 14, of coronary thrombosis.

Edward Ryan, Kingston, Ont., Canada; Queen's University Faculty of Medicine, Kingston, 1889; formerly professor of psychiatry and associate professor of surgery at his alma mater; at one time mayor; served during the World War; in 1927 was appointed director of hospital services for the province of Ontario; formerly superintendent of the Ontario Hospital; died, July 23.

Charles Rex Kennedy * Omaha; University of Nebraska College of Medicine, Omaha, 1905; professor of clinical surgery at his alma mater; fellow of the American College of Surgeons; surgeon to the Nebraska Methodist Episcopal Hospital; division surgeon to the Union Pacific Railroad; aged 56; died, July 29, in Nevis, Minn., of pulmonary edema.

Francis J. Brennan, Oshkosh, Wis.; Marquette University School of Medicine, Milwaukee, 1931; member of the State Medical Society of Wisconsin and the Radiological Society of North America; aged 34; on the staff of the Mercy Hospital, where he died, July 7, of duodenal ulcer, hemorrhage and acute bilateral nephritis.

John A. K. Birchett Sr. * Vicksburg, Miss.; Medical Department of Tulane University of Louisiana, New Orleans, 1891; past president and secretary of the Warren County Medical Society; on the staff of the Vicksburg Infirmary; aged 71; died, July 22, of coronary thrombosis and arteriosclerotic heart disease.

Robert R. Curtis, Temple, Texas; University of Louisville (Ky.) Medical Department, 1894; member of the State Medical Association of Texas; formerly city health officer; on the staff of the Scott and White Hospital; aged 67; died, July 20, in a local hospital, of malignancy and mesenteric thrombosis.

Russell Edwin Olson, Milwaukee; Marquette University School of Medicine, Milwaukee, 1916; member of the State Medical Society of Wisconsin; served during the World War; on the staffs of the Misericordia and St. Joseph's hospitals; aged 44; died, July 14, of portal cirrhosis.

Howard Orville Lienhardt * North Kansas City, Mo.; St. Louis University School of Medicine, 1912; served during the World War; formerly member of the school board; aged 50; on the staff of the Research Hospital, Kansas City, where he died, July 3, of bronchogenic carcinoma.

Wyllys Royce Hodges, Cumberland, Md.; Southern Homeopathic Medical College, Baltimore, 1900; member of the Medical and Chirurgical Faculty of Maryland; on the staff of the Memorial Hospital; aged 64; died, July 14, of coronary sclerosis and diabetes mellitus.

Stuckey Fleetwood McIntosh * Tucson, Ariz.; Tulane University of Louisiana School of Medicine, New Orleans, 1921; at one time secretary of the Chattanooga and Hamilton County (Tenn.) Medical Society; aged 44; died, July 24, at Van Horn, Texas, of heart disease.

Thomas Theodore Sawyer * Kansas City, Mo.; University Medical College of Kansas City, 1907; veteran of the Spanish-American and World wars; aged 59; died, July 25, in the Veterans Administration, Excelsior Springs, of chronic nephritis and hypertension.

Christopher Tuttle Croddy, Portland, Ore.; Rush Medical College, Chicago, 1897; member of the Oregon State Medical Society; aged 75; died, June 26, of angina pectoris, arteriosclerosis and hemiplegia.

Henry Ferrell Carman, Butte, Mont.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1906; aged 63; died, July 24, in Wise River, of cerebral hemorrhage.

William Harry Hawley * College Corner, Ohio; Miami Medical College, Cincinnati, 1885; member of the Indiana State Medical Association; formerly member of the school board; aged 80; died, July 6.

Oscar Clyde Page, Brodnax, Va.; University College of Medicine, Richmond, 1911; member of the Medical Society of Virginia; served during the World War; aged 53; died, July 1, of heart disease.

James Everett Pierpoint, Skidmore, Mo.; Ensworth Medical College, St. Joseph, 1899; member of the Missouri State Medical Association; aged 69; died, July 14, of coronary occlusion.

Leonard S. Krauss, Middletown, Ohio; Ohio Medical University, Columbus, 1895; aged 85; died, July 16, of arteriosclerosis, Parkinson's disease and heart disease.

Dwight Stanley Whittemore, Brockton, Mass.; Boston University School of Medicine, 1887; aged 74; died, June 25, of cerebral thrombosis and arteriosclerosis.

Peter L. Benthack, Chadron, Neb.; Kansas City (Mo.) Homeopathic Medical College, 1899; aged 70; died, June 12, of epithelioma of the lower lip.

Elizabeth Pruin Hofma, Grand Haven, Mich.; Woman's Medical College, Chicago, 1891; aged 78; died, July 2, of myocarditis and arteriosclerosis.

Samuel Houston McMahon, De Ridder, La.; Kentucky School of Medicine, Louisville, 1898; aged 74; died, July 3, of encephalitis.

Daniel Keyworth Cowley, Granby, Que., Canada; McGill University Faculty of Medicine, Montreal, 1880; aged 81; died, July 10.

John R. Holsclaw, Shepherdsville, Ky.; Louisville (Ky.) Medical College, 1875; aged 87; died, June 30, of chronic nephritis.

George L. Hines, Williamsburg, Ohio; Medical College of Ohio, Cincinnati, 1882; aged 81; died, July 15, of senile dementia.

George G. Kreeger, Richmond, Kan.; Kansas City (Mo.) Medical College, 1895; aged 65; died, July 11, of coronary sclerosis.

Thomas G. Howe, Atlanta, Texas; Memphis (Tenn.) Hospital Medical College, 1893; aged 83; died in July of senility.

Jacob Marcus, Boston; Tufts College Medical School, Boston, 1912, aged 53; died, June 22, of hypertension.

Correspondence

CALCIUM METABOLISM AND TEETH

To the Editor:—While there are some problems pertaining to dental caries which remain unsolved, there are innumerable well established facts relating to it which are widely known and generally accepted. Dr. Schour in his article on calcium metabolism and the teeth in *THE JOURNAL* (March 19, p. 870), logically and dispassionately stated these facts and fairly summarized the present status of dental caries. While it is not meant that his studies are complete or final, the chemoparasitic theory to which he subscribes will not be modified and the data on which he bases his conclusions will not be disproved. It was, therefore, regrettable and confusing that an article of such outstanding merit should have been questioned by Dr. McCall (*THE JOURNAL*, July 23, p. 338), particularly since the criticisms were based on so little and as yet controversial evidence.

Since the days of Miller it has been almost universally accepted among scientists that decay begins externally, that the enamel is entirely passive in the process, and that the disease is caused by acids liberated by the bacterial fermentation of carbohydrates.

Periodically during the last decade, certain individuals have made many attempts, unfortunately not based on adequate scientific evidence, to revive the discarded humoral and vital theories of decay. These investigators have postulated that the enamel, through its organic matrix and lamellae, remains under metabolic and physiologic influences throughout life and therefore is not only subject to variations in its resistance to dental caries but exhibits the ability to defend and repair itself actively. The fact that devitalized and normal teeth, as far as the enamel at least is concerned, react pathologically in an identical manner and likewise and to the same extent exhibit susceptibility or immunity to dental caries, together with the fact that there is a reciprocal relationship between tooth density, permeability and caries, should be sufficient evidence to disprove the claims of those who contend that metabolism occurs in formed enamel and that on the efficiency of this process depends the incidence and progress of decay.

More recently the vital humoralists have postulated that alterations of systemic metabolism, secondary to the ingestion of modern food, cause a change in the chemical nature of the saliva, which by altering the local environment permits enamel decalcification and the development of caries. The main evidence on which Dr. McCall takes exception to the article by Schour is predicated on this as yet wholly unproved assumption: that there is a chemical difference between the salivas of caries immune and caries susceptible individuals. To date there has been no satisfactory evidence submitted that there is any difference in chemical composition of the clean saliva of the two groups. On the contrary, the evidence overwhelmingly favors the view that the saliva as it enters the mouth is chemically if not immunologically identical in the two groups.

I disagree with Dr. McCall's contention that pregnancy may influence the development of caries and that hypoplastic enamel is more susceptible to caries than normal enamel. From a review of Dr. McCall's work I have been unable to find any evidence which would justify the conclusion that "evidence is accumulating to show that at any time of life the general metabolism affects the teeth and largely determines whether or not they will decay."

In view of the already widespread acceptance of Schour's views it is somewhat anachronistic and unnecessarily alarming to contend that Schour's "conclusions might, if accepted, have possible unfortunate effects on medical practice." To date no satisfactory evidence has been submitted which would tend to

favor the belief that metabolism occurs in formed enamel; therefore, in view of the really large amount of evidence to the contrary the burden of proof that it does occur must continue, of course, to rest with the exponents of the vital theories.

While it is remotely possible that the theory of chemico-parasitism may eventually prove to be inadequate to explain certain facts pertaining to dental caries, it is apparent that the contentions and evidence presented by McCall do not seriously challenge, much less demand the modification of, Miller's theory of decay.

JULIAN AMBROSE, D.D.S., New York.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

DEATH RATE AND INCOME

To the Editor:—Have you any statistics relative to the comparative death rate in the lower income group (up to \$2,000 or \$2,500) as it is at present and as it was twenty years ago? The statement was made recently that the death rate had declined in the upper income group on account of the better available medical facilities but that the death rate in the lower group was as high as ever.

ROBERT C. JAMIESON, M.D., Detroit.

ANSWER.—No studies comparing the death rates in the lower income classes twenty years ago with the death rates today have been found. Prior to 1930 there were no studies of mortality data according to occupation, and no statistics have been compiled on mortality rates by income classes, except for a few special studies of individual causes of death.

Mortality statistics from the Bureau of the Census show that the death rate has decreased from 15.0 per thousand in 1910 to 10.9 per thousand in 1935, or a decrease of 27.3 per cent. If the upper limit of the low income group is taken as \$2,500, nearly 20,000,000 families, or 71 per cent of all families in the United States, would belong to this group (America's Capacity to Consume, Brookings Institution). Consequently the decline in the death rate during the twenty-five year period from 1910 to 1935 could not be accounted for by a decrease in mortality rate for the persons in the income group above \$2,500 alone.

Likewise the Metropolitan Life Insurance Company, in a study of the mortality rate among its industrial policyholders, showed a decline of 35.8 per cent in the mortality rate during the period from 1911 to 1938 (Statistical Bulletin, Metropolitan Life Insurance Company, January 1938). The industrial policyholders of the Metropolitan were largely persons in the lower income brackets of the urban population.

From the foregoing it appears rather certain that the death rate in the lower income group has been steadily decreasing during the past twenty years.

A special study of mortality statistics according to occupation was made for ten states which in a certain way indicates the mortality rate according to the economic status of the majority in the occupational group (Death Rates by Occupation, by J. S. Whitney, based on United States Census Bureau data for 1930). For example, the mortality rate for professional men in 1930 was 7.0 per thousand, while for unskilled workers it was 13.1 per thousand.

No similar study has been made since to show whether the mortality in the occupational groups with a relatively high average economic status is declining faster than the mortality rate for occupational groups with a lower economic status. Furthermore, mortality studies according to occupational groups do not accurately show the mortality according to economic status, because the occupational hazards have a greater effect on the mortality rate than the differences in the standards of living; that is to say, a group of unskilled workers with an average income of \$100 a month would be more likely to have a higher death rate than a group of professional workers with an average income of \$100 a month, chiefly because of the hazards of the occupations followed by unskilled workers.

The statement that the death rate in the upper income group is lower on account of the better available medical facilities is inaccurate because many other factors are involved. As an example, *Public Health Reports* for Sept. 2, 1934, shows the results of an experiment in Liverpool, England, where the death rate from all causes for a certain slum area was reduced from 37.0 per thousand to 26.6 per thousand after the area was rebuilt with better homes and improved sanitation; with few exceptions the same population remained in the area. Likewise, agricultural workers have the lowest mortality rate of any occupational group, which indicates that occupational conditions and the standard of living are important factors in reducing mortality.

The United States Public Health Service has made a great many sample studies of morbidity and mortality in relation to economic status. In general, these studies indicate that higher illness and mortality rates among the poor are caused primarily by factors such as crowded housing conditions, lack of adequate food and clothing, and occupational hazards. The availability of medical care is also a factor.

ASCENDING PARALYSIS AND POSSIBLE SPINAL CORD COMPRESSION

To the Editor:—A man aged 48, whose present complaint is increasing paralysis of the spastic type for the last six months, has entirely lost the action of his legs. He can move both arms slightly and when he does so there is a decided tremor. Knee, ankle, biceps, triceps are all hyperactive and equal. Ankle clonus is bilateral; there is a suggestive right Babinski; the Hoffmann thumb sign is present in both hands; the abdominals are present, the cremasteric is decreased; vibration sense is normal; likewise pain, temperature and tactile sense are normal. There is no slurring of speech; the eye grounds are normal; there is no bitenporal pallor or nystagmus; the facial expressions are normal; there is no cranial nerve involvement, headache, double vision or difficulty in swallowing. X-ray examination of the skull shows questionable early calcification of the pituitary; x-ray examination of the cervical spine shows a normal condition. The blood count, red and white, is within normal limits; the blood and spinal Wassermann reactions are negative. The spinal fluid cell count shows 2 cells; sugar (spinal fluid) 75; protein, 57. The patient is clear mentally. There is no history of injury. Occasionally there is a rise in temperature of 1 degree. The urine is essentially normal. The paralysis began with the lower extremities and is progressing upward. A neurologist is as puzzled as I am. M.D., N. Y.

ANSWER.—Increasing spastic paralysis in a man of 48, beginning in the legs and ultimately involving the arms, is suggestive of compression of the spinal cord. The facts, as given, indicate that this possibility has not been entirely ruled out. The level of the lesion is at least as high as the fifth cervical segment and the practical question arises as to whether or not evidence is present of disease of the first four cervical vertebrae. Although the roentgenograms of the cervical spine are said to show a normal condition, particular care should be directed toward a complete examination of these four vertebrae—not by any means an easy task. Tuberculous osteitis, secondary carcinoma or other neoplasms such as sarcoma, myeloma or lymphoblastoma are easily overlooked unless the roentgenograms are exceptionally good. There is evidence, moreover, of a partial block in the spinal fluid in that the total protein is 57 mg., somewhat higher than the normal limit. Unfortunately the record does not state anything with regard to the hydrodynamics of the cerebrospinal fluid, particularly the Queckenstedt test. In high spinal cord tumors this test is not of as much value as in those lower down. Nevertheless, evidence along these lines should be sought for. Of particular value in an obscure case would be a combined cistern and lumbar puncture, with a record of both responses to jugular compression and also a comparison of the amount of protein from both loci. If any signs of block should be found, an attempt should be made to visualize the exact level of the lesion, and possibly its nature, by the injection of iodized oil into the cistern, allowing it to run down in the spinal subarachnoid space. By such an examination, tumor or adhesive arachnoiditis might be disclosed. Pachymeningitis, moreover, in this region is certainly to be considered. It does not necessarily need to be on a syphilitic basis. Should evidence for a block in the cerebrospinal fluid be obtained by examinations, laminectomy with exposure of the area would be the treatment of choice.

Without sensory changes or disturbance of the sphincters, intramedullary cord tumor is unlikely, nor would one expect to find an intrinsic degenerative disease like syringomyelia. The lack of any involvement of the cranial nerves, plus the presence of the abdominal reflexes, along with the patient's age, make a diagnosis of multiple sclerosis unlikely.

It is therefore clear that, before a definite diagnosis can be made, the patient needs additional examinations. Such exami-

nations as the combined puncture, the injection of iodized oil and the reading of the results by the radiologist require a good deal of skill and should not be undertaken unless a thorough understanding of the value of these examinations is available. In view of the patient's progressive paralysis, such examinations are entirely justified and operation should not be overlooked as an important means of treatment should the examinations disclose a definite compression of the spinal cord.

EHLERS-DANLOS SYNDROME

To the Editor:—Please send information concerning the Ehlers-Danlos syndrome: symptoms and treatment, if any.

ERNEST B. HANAN, M.D., Bolivar, Mo.

ANSWER.—The Ehlers-Danlos syndrome is congenital and of rare occurrence. Its subjects are not unusually objects of curiosity and are therefore exploited in cheap museums and sideshows.

There are essentially three parts to the syndrome. The skin is abnormally elastic, so that it may be pulled out to excessive distances. The favorite sites to elicit this increased elasticity are at the elbows and knees. The skin may snap back into place like a rubber band after it is pulled. Other times there is a more gradual resumption of the original outline of the skin. Noteworthy histologic changes of the skin seen in the hyperelastic regions are tortuosity of the blood vessels and undulations and increase in the elastic elements. The second cardinal feature of this syndrome is the overextensibility of the joints, especially at the base of the thumb. Finally the skin is easily injured to form thin atrophic scars. These occur most frequently about joints, especially at the elbows and knees. The type of scarring is characteristic and is the most commonly encountered sign of the triad. It is more frequent that individual signs occur alone or in combination with one other. More rarely the full syndrome of three signs appears.

Several congenital anomalies have been associated and confused with the Ehlers-Danlos syndrome. Dermatolysis, in which there are loose aprons of skin, is not to be identified with this syndrome. Related to it but not identical is the dystrophic variety of epidermolysis bullosa. The connection of Recklinghausen's disease and the Ehlers-Danlos syndrome has been discussed in the literature.

There is no suggested therapy. It is a permanent developmental anomaly.

TETANUS ANTITOXIN OR CORONARY THROMBOSIS AS CAUSE OF DEATH

To the Editor:—A patient cut one finger of one hand on a nail, Feb. 14, 1938. On the same day he was given first aid treatment and 1,500 units of tetanus antitoxin, first having been tested intradermally. Approximately one week later he had an attack of syncope, associated with precordial pain, weakness, dyspnea and loss of consciousness. At this time the family noticed that he had a generalized erythematous rash and he was taken to a hospital where he was told that he had a serum reaction. The man continued to work and approximately one week later had a second attack, when he complained of pain in his chest followed by a rapid loss of consciousness. He died in a few minutes. The only abnormalities at the autopsy were a moderate coronary sclerosis and a recent myocardial infarct, which was along the course of one of the branches of the left coronary artery. On microscopic examination it was found that the infarct had occurred from ten to fourteen days before death. The pathologist reported that the man died of coronary spasm, which was sufficient to cause death because of the already damaged infarcted left ventricle, that there was a definite connection between the tetanus antitoxin and the cardiac condition and symptoms and that he believed the tetanus antitoxin was definitely a contributory factor in the death of this man. I have talked with cardiologists who do not believe that the tetanus antitoxin was a contributing factor. Please give your opinion, with reference to the literature if there is any. M.D., Texas.

ANSWER.—A man, age unstated, had an attack of syncope, precordial pain and other symptoms, which was followed by a second and similar but fatal attack about one week later. Coronary sclerosis and myocardial infarction were demonstrated and evidently it concerned a fairly typical case of fatal coronary disease. The question is raised whether an injection of tetanus antitoxin had exercised a determining effect on the course of events. The statement mentions that an erythematous rash was present when the first heart attack came on about one week after the antitoxin was given. In view of the great variety of conditions under which a serum reaction set in it is purely speculative whether the alleged serum reaction had any part in the first attack in this case. That the serum reaction had any direct part in the second and fatal attack seems quite unlikely,

b. cause it occurred a week or so after the reaction. There is no other evidence available except the apparent coincidence of the serum reaction and the first attack to support the statement that "the tetanus antitoxin was definitely a contributing factor in the death" of the patient.

AREA FOR INJECTION OF PERTUSSIS VACCINE

To the Editor:—Why is the Sauer pertussis vaccine given in the arm alone? Is there some reason for injecting the vaccine in different areas of the arm or would any subcutaneous injection be all right?

CLARENCE M. O'HORA, M.D., Beaver Dam, Wis.

ANSWER.—In 1925 Madsen reported on the injection of *Haemophilus pertussis* vaccine containing 10,000,000,000 bacilli per cubic centimeter, a total dose of 2.2 cc. (0.5, 0.7 and 1 cc. at three day intervals). This dose usually failed as an immunizing agent, but Danish clinicians and health officers observed a milder course and fewer deaths in patients who had had the vaccine. They believed that their best results occurred in those who had a transient local reaction at the time of injection. In his vaccination against whooping cough, Sauer since 1928 has used for children under 2 years of age a total dose of 8 cc. (2, 3 and 3 cc. at weekly intervals), a total of 80,000,000,000 bacilli. He believes that a better immunity response occurs when the injections are given just under the skin. The freshly isolated cultures are grown on human blood mediums to exclude anaphylaxis and sensitization due to alien proteins.

The upper parts of the arms are the logical site for the superficial injection of such quantities of concentrated vaccine. The arms were probably chosen because the desired local reaction (immediate blanching, subsequent erythema) would cause the least inconvenience there. It is less likely to be scratched than if given on the trunk. The buttocks would entail unnecessary hazards, because of the danger of abscess from fecal contamination or excoriated skin from ammoniacal diapers.

Infection of the upper arms will not occur if the syringe and needle are sterilized by heat (oven at 250 F. for one hour, or boiling), vial cap and site thoroughly cleansed with ethyl (not "rubbing") alcohol. Wet dressings should not be applied for local redness.

PERSISTENT LEUKOPENIA

To the Editor:—Have there ever been reported in the literature such conditions as anomalies of the hemopoietic system in which the normal white cell count is extremely low? A man aged 23 on repeated examinations is found to have a white cell count of 1,500, the lowest count being 1,100 and the highest 2,000. The only significance of the differential counts is the finding of an increased number of band forms, varying from 11 to 34. The other components of the blood have been normal. The patient feels well and repeated physical examinations in the last two months have revealed nothing of significance to lead one to suspect leukemia or a true agranulocytosis. The patient was admitted to the hospital because of the low count found on a routine check-up.

M.D., Rhode Island.

ANSWER.—There occur occasionally physiologic leukopenic states lasting for years in persons in whom no primary bone marrow or secondary causative tissue or organ disorder can be found (Doan, C. A.: *The Neutropenic State*, *THE JOURNAL*, July 16, 1932, p. 194). In such cases intercurrent infections are accompanied by adequate granulocytic leukocytoses; the duration and severity of such illnesses is no greater than in those cases in which an average interim total white cell count of between 5,000 and 10,000 is shown, and bone marrow studies reflect no disturbance in the normal myeloid-erythroid ratio or in the physiologic maturation pattern of the myelocytes. Such cases reported in the medical literature, however, usually have shown a total white count maintained between 2,000 and 3,500 with normal differential white cell relationships, both qualitatively and quantitatively.

When the total white count remains persistently below 2,000 and on repeated observations may even occasionally fall below 1,000, without other readily detected signs or symptoms, as in the case cited, one must seriously consider an early Banti's syndrome. The first evidence of this disease entity may be a profound asymptomatic leukopenia. Sooner or later the spleen will become palpable and one or more of the usual liver function tests, including the bromsulphalein dye, the galactose tolerance and the hippuric acid excretion tests, will reflect hepatic damage. The bone marrow shows no inhibition or diminution of normal hemopoiesis and unless and until gastrointestinal hemorrhage occurs, occult or gross, there will be no anemia and no significant platelet changes. The leukopenia would appear to depend on a specific splenic sequestration of leukocytes because following successful splenectomy in such cases the total white count again becomes normal. There are no pathognomonic tests or

physical signs in the establishment of Banti's syndrome early. The diagnosis must be made by eliminating all other possible mechanisms for the leukopenia, and the alert physician may occasionally advise prompt splenectomy in order to avert a massive esophageal hemorrhage, which so often is the first sign of the far advanced disease. Successful splenectomy in this condition depends on early diagnosis before perisplenic adhesions and venous dilations make removal of the spleen impossible.

Leukopenia rarely, if ever, is the initial blood finding in incipient hypoplastic or aplastic anemia. When present, it is distinctly a granulopenic leukopenia and practically always is preceded or accompanied by a more or less marked thrombocytopenia or/and anemia.

True agranulocytosis also is reflected by a granulopenic white count, with absolute marrow myelopenia and immaturity, and usually is followed promptly by characteristic clinical symptoms.

Aleukemic leukemia likewise is seldom asymptomatic or without physical signs, and the quality and relative disproportionate increase of the leukemic cells should be diagnostic.

DIAGNOSIS IN SPASTIC ATAXIA

To the Editor:—A man aged 65 had pneumonia six years ago. During his convalescence he noticed stiffness, numbness and pricking sensations of his legs and feet without pain. He has had difficulty since in walking in the dark, stumbling easily, and the leg symptoms have persisted. He now has pain in the legs and his hands feel as if they were asleep. He complains of tightness around the lower part of the abdomen, beltlike in character. He weighs 172 pounds (78 Kg.) and has a blood pressure of 174/70 and a regular pulse of 100. The Romberg sign is present. He has loss of vibratory sense from the waist down. The knee jerks are slightly exaggerated; the Babinski reflex is present; abdominal reflexes are lost. There is no nystagmus. The blood count reveals 4,180,000 erythrocytes, 7,800 leukocytes, a normal differential and hemoglobin of 13 Gm. The blood and spinal fluid Wassermann, Kline and Kahn reactions are negative. There is a slight increase of globulin in the spinal fluid. The colloidal gold curve is 1112321000. There are no other symptoms or positive physical signs. Do you agree that the most probable diagnosis is subacute combined sclerosis of the spinal cord? With this blood picture, without benefit of gastric analysis, can I say that he has no primary anemia? With no history of syphilis or of observations other than those given, can I say that he does not have syphilis? What may I offer him in the way of prognosis and therapy? How should the colloidal gold curve be interpreted?

REID P. JOYCE, M.D., Ashland, Ohio.

ANSWER.—The patient has the signs and symptoms of spastic ataxia due to involvement of the posterior and lateral columns of the spinal cord (thoracic cord?). The most probable causes of this condition may be (1) pernicious anemia resulting in subacute combined cord degeneration; (2) cerebrospinal sclerosis (arteriosclerotic); (3) pneumonia; (4) cord tumor; (5) avitaminosis. To make a diagnosis of subacute combined sclerosis of the spinal cord one should find achylia gastrica (no free acid in the stomach contents). If achylia gastrica is not found, the most likely diagnosis is a pneumonic myelitis. One should do a careful manometric study of the spinal fluid to rule out a block due to a tumor. The second question cannot be answered. In 30 per cent of cases of subacute combined cord degeneration the blood picture is normal. In six years, however, there should have been a change in the blood picture if one is dealing with a pernicious anemia, unless the patient is being treated with large doses of liver. From the evidence submitted one can be fairly confident that the patient does not have syphilis. The prognosis is doubtful. The patient should be placed at absolute bed rest for a period of six to eight weeks and large doses of liver with vitamins A, B₂ and G given three times weekly by intramuscular injection. Reeducation exercises are suggested for the sensory ataxia. The colloidal gold curve is not significant of any condition. It should be considered as an atypical normal.

TREATMENT OF CONGENITAL CLUBFOOT

To the Editor:—What is the best therapy for congenital clubfoot (rigid contracted arch)? What percentage of cures are effected when the usual surgical procedures are employed?

ROBERT MONFORT, M.D., Onaway, Mich.

ANSWER.—Treatment for congenital clubfoot depends on the type of deformity, which may be varus, valgus, calcaneus, equinus or a combination of two or more of these, and also on the age of the child and the methods of treatment which have been used previously. Since the patient concerned is said to have a rigidly contracted arch, it may be safely assumed that it is not a newborn infant. Approximately 75 per cent of clubfoot deformities are of the talipes equinovarus type. When early correction has not been successful or the condition has been neglected until the deformity has become rigidly fixed with a

contracted arch, an operation is indicated. This may include section of the flexor hallucis longus tendon, posterior capsulotomy of the ankle, lengthening of the achilles tendon, or section of the adductor brevis tendon and of the plantar fascia near its insertion into the os calcis. These are the structures, either static or dynamic, which are responsible for maintenance or recurrence of the deformity. After these operative procedures the foot should be manipulated while the patient is still under the anesthetic and a cast applied to maintain a position of over-correction. In some instances the number of operative procedures may be less than those mentioned and in other cases more. For the patient 6 years or younger, this course of treatment may be found adequate in a reasonably high percentage of cases. For patients more than 6 years of age, one has to consider the advisability of arthrodesis of some of the proximal tarsal joints. This may be indicated when there is severe deformity of the bones of the foot because of long continued malposition.

The surgeon should constantly keep in mind the fact that, while it may not be difficult to manipulate and correct the position of a clubfoot, the factors of muscle imbalance and ligament contractures must be treated in order to prevent prompt recurrence with even more serious deformity after the restraint of the cast has been removed.

Some authors have stated that 60 per cent of these cases will recur when only manipulation and cast are used in the treatment. References:

- Compere, E. L.: Congenital Talipes Equinovarus, *S. Clin. North America* 15:767 (June) 1935.
McCauley, John C., and Krida, Arthur: The Early Treatment of Equinus in Congenital Clubfoot, *Am. J. Surg.* 22:491 (Dec.) 1933.

ESTIMATION OF SPINAL FLUID PROTEIN

To the Editor:—What is the best technic for estimating the total protein in the spinal fluid? ROBERT M. HARBIN JR., M.D., Rome, Ga.

ANSWER.—The amount of protein present in normal cerebrospinal fluid is so small (under 0.1 per cent) that its accurate estimation is a matter of some difficulty. Several different procedures may be followed: 1. The total nitrogen, and nonprotein nitrogen after Folin-Wu tungstic acid precipitation, may be determined in the spinal fluid by the micro Kjeldahl method, the difference between the two determinations taken as representing the protein nitrogen and multiplied by the factor 6.25. 2. The protein may be precipitated by tungstic acid and the amount of this precipitate estimated by either (a) the micro Kjeldahl nitrogen estimation or (b) the use of Folin's tyrosine reagent (Ling, S. M.: *J. Biol. Chem.* 69:397 [Aug.] 1926) and the amount of protein calculated by employing suitable factors [(a) 6.25 and (b) 19.1]. 3. Or more simply by precipitating the protein with some reagent such as sulfosalicylic acid and determining the amount of this precipitate nephelometrically or turbidimetrically. The last procedure was employed by Denis and Ayer (*Arch. Int. Med.* 26:436 [Oct.] 1920) with satisfactory results and has since been used by many workers. Marjorie R. Mattice (Chemical Procedures for Clinical Laboratories, Philadelphia, Lea & Febiger, 1936, p. 387) states that she has found this method to check with the Kjeldahl procedure. The Dennis-Ayer method would appear to be the simplest satisfactory method of estimating spinal fluid protein.

SECOND COURSE OF MALARIA FOR DEMENTIA PARALYTICA

To the Editor:—The members of the staff of the hospital with which I am connected have been having some arguments of late as to the efficacy of repeating malarial therapy in dementia paralytica. Some claim that it is useless to give it more than once and others that it should be repeated. What is your opinion? M.D., Indiana.

ANSWER.—The reports which appeared in the literature for several years after Wagner von Jauregg suggested the use of malaria indicated that a second course of malaria would occasionally produce satisfactory clinical results when the first course had been unsuccessful. However, subsequent experience has not substantiated this observation and it is now generally accepted that the second malarial course will not be more successful than the first.

It is usually impossible to produce a second febrile course from reinoculation with malaria that will produce more than one or two attacks of fever, because these patients tend to arrest the malaria spontaneously. Although the blood may show *Plasmodium vivax* following inoculation the second time, the chills and fever do not develop. If a patient does not derive

clinical or serologic benefit from a course of malaria, it is of more advantage to use one of the fever producing machines for the second fever course rather than to attempt to use the malaria a second time. Irrespective of the type of fever therapy employed, the use of arsphenamine and a bismuth compound or tryparsamide and a bismuth compound is indicated after the fever course.

CAR SICKNESS: PAROXYSMAL LABYRINTHINE DISEASE OR EPILEPSY

To the Editor:—A boy aged 12 is subject to car sickness, depending on the anxiety with which he travels to a certain destination by automobile or trolley car. He becomes pale and nauseated and is slightly uncomfortable even after riding merely a half hour. He is not so likely to become car sick while riding in an omnibus. Physical and otologic examinations reveal nothing to account for this. His eyes have recently been refracted and he is wearing proper glasses. Casual riding on a bicycle has not given him any trouble. Is there any danger from a fall if bicycle riding causes a feeling similar to car sickness? I myself have not known of such an instance, yet a neurologist has warned the boy against bicycle riding. On the other hand, it is likely that bicycling would accustom a boy to traveling so that car sickness would be mitigated when he rides in an automobile or trolley car? M.D., Pennsylvania.

ANSWER.—The diagnosis appears to be paroxysmal labyrinthine disease. In this condition the only objective finding is usually an irritable labyrinth. If this is the case there is no danger from a fall while riding a bicycle. One must be sure that one is not dealing with epilepsy. That is why the neurologist in all probability advised against riding a bicycle. It is suggested that this boy be placed on a salt free diet and given from 1.3 to 1.6 Gm. (20 to 25 grains) of ammonium chloride in a capsule three or four times daily for a period of ten days or two weeks. This condition is analogous to sea sickness, air sickness and elevator sickness.

OAK BALM SUPPOSITORIES

To the Editor:—What is the present status of the Oak Balm (Hager) Company, South Bend, Ind.?

ROBERT MONTFORT, M.D., Onaway, Mich.

ANSWER.—No analysis has been made of "Oak Balm" by the American Medical Association. Some years ago the state chemists of North Dakota analyzed Oak Balm and reported that these suppositories were composed chiefly of boric acid and alum, in a cacao base. The chemists added that "tannin was not detected, therefore no oak constituent was present." As there is nothing to prevent "patent medicine" exploiters from changing the composition of their products overnight, we are unable to state whether the ingredients given above represent the present composition of this nostrum.

LEFT HANDEDNESS IN CHILD

To the Editor:—What is the present status of treatment of left-handedness in a child? A boy aged 3 has been using his left hand in picking up and holding objects and now uses this hand to eat with almost exclusively. His use of the right hand seems awkward. Should any attempt be made to correct this? If so, what is the best procedure? M.D., Pennsylvania.

ANSWER.—It is considered unwise to attempt to coerce a distinctly left-handed child to use his right hand as the dominant one. There is some justification in making an exception in training the child to use the right hand in eating, since this avoids later social discomfort. No measures more energetic than persistent encouragement in the use of the right hand for eating are justified.

TRAUMA AND PRIAPISM

To the Editor:—I have a case of priapism which I believe is on the basis of trauma and thrombophlebitis of the corpora cavernosa and spongiosum. The patient was injured about two weeks ago while attempting intercourse while under the influence of alcohol. The priapism came on at once and has existed up to the present. Neurologic consultation has ruled out cord lesion, the Kahn reaction is negative, and blood studies rule out a leukemia. Free use of sedatives and narcotics have failed to influence the condition, as have spinal anesthesia, high voltage roentgen therapy and diathermy. The therapeutic measure of greatest value to date has been sitz baths. I would appreciate any suggestions as to the diagnosis or treatment. M.D., Pennsylvania.

ANSWER.—There is no doubt from the history of the case that it belongs to the traumatic group. The treatment should be incisions under absolute asepsis to remove any blood clots and to allow free drainage of the exudate. The incisions should be made into the most turgid portions of the penis.

Medical Examinations and Licensure

COMING EXAMINATIONS

STATE AND TERRITORIAL BOARDS

ALABAMA: Montgomery, June 20-22. Sec., Dr. J. N. Baker, 517 Dexter Ave., Montgomery.

ARKANSAS: *Medical (Regular)*. Little Rock, Nov. 3-4. Sec., State Medical Board of the Arkansas Medical Society, Dr. L. J. Kosminsky, Texarkana. *Medical (Eclectic)*. Little Rock, Nov. 3. Sec., Dr. Clarence H. Young, 1415 Main St., Little Rock. *Basic Science*. Little Rock, Nov. 7. Sec., Mr. Louis E. Gebauer, 701 Main St., Little Rock.

CALIFORNIA: *Written examination*. Sacramento, Oct. 17-20. *Reciprocity*. Los Angeles, Nov. 16. Sec., Dr. Charles B. Pinkham, 420 State Office Bldg., Sacramento.

COLORADO: Denver, Oct. 5-7. Sec., Dr. Harvey W. Snyder, 831 Republic Bldg., Denver.

CONNECTICUT: *Basic Science*. New Haven, Oct. 8. *Prerequisite to license examination*. Address State Board of Healing Arts, 1895 Yale Station, New Haven. *Medical (Regular)*. Hartford, Nov. 8-9. Sec., Dr. Thomas P. Murdock, 147 W. Main St., Meriden. *Medical (Homoeopathic)*. Derby, Nov. 8-9. Sec., Dr. Joseph H. Evans, 1488 Chapel St., New Haven.

DELAWARE: Dover, July 11-13. Sec., Medical Council of Delaware, Dr. Joseph S. McDaniell, 229 S. State St., Dover.

DISTRICT OF COLUMBIA: *Basic Science*. Washington, Dec. 26-27. *Medical*. Washington, Jan. 9-10. Sec., Commission on Licensure, Dr. George C. Ruhland, 203 District Bldg., Washington.

FLORIDA: Jacksonville, Nov. 14-15. Sec., Dr. William M. Rowlett, Box 786, Tampa.

GEORGIA: Atlanta, Oct. 11-12. Joint-Sec., State Examining Boards, Mr. R. C. Coleman, 111 State Capitol, Atlanta.

HAWAII: Honolulu, Oct. 10-13. Sec., Dr. James A. Morgan, 48 Young Bldg., Honolulu.

IDAHO: Boise, Oct. 4-5. Commissioner of Law Enforcement, Hon. J. L. Balderston, 205 State House, Boise.

ILLINOIS: Chicago, Oct. 18-20. Superintendent of Registration, Department of Registration and Education, Mr. Homer J. Byrd, Springfield.

INDIANA: Indianapolis, June 20-22. Sec., Board of Medical Registration and Examination, Dr. J. W. Bowers, 301 State House, Indianapolis.

IOWA: *Basic Science*. Des Moines, Oct. 11. Corres. Sec., Mr. H. W. Greffe, Capitol Bldg., Des Moines.

KANSAS: Topeka, Dec. 13-14. Sec., Board of Medical Registration and Examination, Dr. J. F. Hassig, 905 North 7th St., Kansas City.

KENTUCKY: Louisville, Dec. 6-8. Sec., State Board of Health, Dr. A. T. McConnack, 620 S. Third St., Louisville.

MAINE: Portland, Nov. 8-9. Sec., Board of Registration of Medicine, Dr. Adam P. Leighton, 192 State St., Portland.

MARYLAND: *Medical (Regular)*. Baltimore, Dec. 13-16. Sec., Dr. John T. O'Mara, 1215 Cathedral St., Baltimore. *Medical (Homoeopathic)*. Baltimore, Dec. 13-14. Sec., Dr. John A. Evans, 612 W. 40th St., Baltimore.

MASSACHUSETTS: Boston, Nov. 8-10. Sec., Board of Registration in Medicine, Dr. Stephen Rushmore, 413-F State House, Boston.

MICHIGAN: Lansing, Oct. 12-14. Sec., Board of Registration in Medicine, Dr. J. Earl McIntyre, 202-3-4 Hollister Bldg., Lansing.

MINNESOTA: *Basic Science*. Minneapolis, Oct. 4-5. Sec., Dr. J. Charnley McKinley, 126 Millard Hall, University of Minnesota, Minneapolis. *Medical*. Minneapolis, Oct. 18-20. Sec., Dr. Julian F. Du Bois, 350 St. Peter St., St. Paul.

MISSISSIPPI: *Reciprocity*. Jackson, December. Asst. Sec., State Board of Health, Dr. R. N. Whitfield, Jackson.

MISSOURI: Kansas City, Oct. 18-20. State Health Commissioner, Dr. Harry F. Parker, State Capitol Bldg., Jefferson City.

MONTANA: Helena, Oct. 4. Sec., Dr. S. A. Cooney, 216 Power Block, Helena.

NEBRASKA: *Basic Science*. Lincoln, Oct. 4-5. *Medical*. Lincoln, Nov. 25-26. Dir., Bureau of Examining Boards, Mrs. Clark Perkins, State House, Lincoln.

NEVADA: Carson City, Nov. 7-9. Sec., Dr. John E. Worden, Capitol Bldg., Carson City.

NEW JERSEY: Trenton, Oct. 18-19. Sec., Dr. James J. McGuire, 28 W. State St., Trenton.

NEW MEXICO: Santa Fe, Oct. 10-11. Sec., Dr. Le Grand Ward, 135 Palace Ave., Santa Fe.

NORTH CAROLINA: *Reciprocity*. December. *Examination*. Raleigh, June 19. Sec., Dr. William D. James, The Hamlet Hospital, Hamlet.

NORTH DAKOTA: Grand Forks, Jan. 3-6. Sec., Dr. G. M. Williamson, 4½ S. Third St., Grand Forks.

OKLAHOMA: *Basic Science*. Oklahoma City, Nov. 30. Sec. of State, Hon. Frank C. Carter, State Capitol Bldg., Oklahoma City. *Medical*. Oklahoma City, Dec. 14. Sec., Dr. James D. Osborn Jr., Frederick.

OREGON: *Medical*. Portland, Oct. 5. Sec., Dr. Joseph F. Wood, 509 Selling Bldg., Portland. *Basic Science*. Portland, Nov. 19. Sec., State Board of Higher Education, Mr. Charles D. Byrne, University of Oregon, Eugene.

PENNSYLVANIA: Philadelphia, January. Sec., Board of Medical Education and Licensure, Dr. James A. Newpher, 400 Education Bldg., Harrisburg.

RHODE ISLAND: Providence, Oct. 6-7. Chief, Division of Examiners, Mr. Robert D. Wholey, 366 State Office Bldg., Providence.

SOUTH CAROLINA: Columbia, Nov. 8. Sec., Dr. A. Earle Boozer, 505 Saluda Ave., Columbia.

SOUTH DAKOTA: Pierre, Jan. 17-18. Director of Medical Licensure, Dr. B. A. Dyar, State Board of Health, Pierre.

VERMONT: Burlington, Feb. 14. Sec., Board of Medical Registration, Dr. W. Scott Nay, Underhill.

VIRGINIA: Richmond, Dec. 14-16. Sec., Dr. J. W. Preston, 30½ Franklin Road, Roanoke.

WEST VIRGINIA: Bluefield, Oct. 31-Nov. 2. Sec., Public Health Council, Dr. Arthur E. McClue, State Capitol, Charleston.

WISCONSIN: Madison, Jan. 10-14. Sec., Dr. Henry J. Gramling, 2203 S. Layton Blvd., Milwaukee.

WYOMING: Cheyenne, Oct. 3. Sec., Dr. G. M. Anderson, Capitol Bldg., Cheyenne.

NATIONAL BOARD OF MEDICAL EXAMINERS SPECIAL BOARDS

Examinations of *Special Boards* were published in THE JOURNAL, September 24, page 1235.

Texas June Examination

Dr. T. J. Crowe, secretary, Texas State Board of Medical Examiners, reports the written examination held at San Antonio, June 20-22, 1938. The examination covered twelve subjects and included 120 questions. An average of 75 per cent was required to pass. One hundred and ninety-two candidates were examined, 176 of whom passed and sixteen failed. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
Rush Medical College.....	(1937)		76.7
School of Med. of the Division of Biological Sciences..	(1935)		84
Tulane University of Louisiana School of Medicine....	(1931)		81.6
Harvard Univ. Medical School..	(1932) 81, (1934) 84.3, (1936)		84.6
Creighton University School of Medicine.....	(1937)		84.5
Columbia Univ. College of Physicians and Surgeons....	(1938)		82
University of Oklahoma School of Medicine.....	(1938)		77.6
University of Pennsylvania School of Medicine.....	(1938)		81
Baylor University College of Medicine.....	(1937)		76.9
79, 85, (1938) 75.4, 75.5, 76.8, 78, 78, 78.9, 79, 79, 79, 79.8, 79.9, 80, 80.4, 80.4, 80.6, 80.9, 81, 81, 81.2, 81.4, 81.5, 81.5, 81.6, 81.8, 81.9, 82, 82.1, 82.1, 82.3, 82.5, 82.7, 83, 83, 83.1, 83.2, 83.2, 83.5, 83.6, 84, 84, 84.2, 84.2, 84.2, 84.3, 84.5, 84.6, 85, 85, 85, 85, 85.1, 85.2, 85.3, 85.3, 85.6, 86, 86, 86.1, 86.3, 86.5, 86.5, 86.6, 86.7, 86.9, 89, 89.4, 91			
University of Texas School of Medicine.....	(1937)		81.7
(1938) 76.6, 77.3, 77.6, 78.4, 78.4, 78.5, 79.3, 79.3, 79.5, 79.5, 79.9, 80, 80, 80, 80.3, 80.3, 80.4, 80.5, 80.5, 80.7, 80.7, 80.8, 80.8, 81, 81, 81.1, 81.2, 81.2, 81.2, 81.3, 81.4, 81.4, 81.4, 81.5, 81.8, 81.9, 81.9, 81.9, 82, 82, 82.1, 82.3, 82.3, 82.3, 82.5, 82.5, 82.7, 82.9, 82.9, 83, 83, 83.3, 83.5, 83.9, 84, 84.5, 84.5, 84.8, 84.8, 85.4, 85.6, 85.7, 86, 86.1, 86.3, 86.3, 86.5, 86.6, 86.6, 87.5, 88.1			
McGill University Faculty of Medicine.....	(1938)		75.6
Osteopaths*			75.3
76.5, 77, 77, 77.7, 77.7, 78.9, 79.1, 80.2, 80.3, 81.1, 81.2, 81.4, 81.5, 82.6, 82.8, 83.6, 85.4			

School	FAILED	Year Grad.	Number Failed
University of Arkansas School of Medicine.....			1
Creighton University School of Medicine.....			1
Baylor University College of Medicine.....			1
University of Texas School of Medicine.....			3
Osteopaths*			10

One hundred and six applicants were licensed by reciprocity and one applicant was licensed by endorsement on July 30. The following schools were represented:

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
University of Arkansas School of Medicine (1932), (1935), (1936), (1937, 4), (1938) Arkansas			
College of Medical	(1931)		California
University of Colorado	(1937)		Colorado
University of Georgia	(1924)		New York
University of Georgia School of Medicine.....	(1934)		Georgia
Chicago College of Medicine and Surgery.....	(1911)		Indiana
Loyola University School			Illinois
Northwestern University			Illinois
(1923) Kansas, (1934, 2)			Iowa
University of Illinois College of Medicine.....	(1925)		
State University of Iowa College of Medicine.....	(1928)		
University of Kansas School of Medicine (1925), (1926), (1936), (1937) Kansas			
Kentucky School of Medicine.....	(1904)		Oklahoma
Kentucky University Medical Department.....	(1906)		Kentucky
Louisiana State University Medical Center.....	(1936)		Georgia
(1937), (1938, 2) Louisiana			
Tulane University of Louisiana Medical Department..	(1912)		Louisiana
Tulane Univ. of Louisiana School of Medicine (1928), (1931)			Mississippi
(1932) Alabama, (1936, 5), (1937, 5) Louisiana			
Harvard University Medical School.....	(1935)		Maine
Univ. of Michigan Dept. of Medicine and Surgery..	(1910)		Michigan
University of Michigan Medical School.....	(1931)		Minnesota
(1933) New York, (1928), (1931), (1937) Michigan			
Univ. of Minnesota Medical School (1933) Minnesota, (1935)			Illinois
Barnes Medical College, Missouri.....	(1902)		Illinois
University of Nebraska College of Medicine.....	(1929)		Kansas
(1933), (1937) Nebraska			
Cornell University Medical College.....	(1934)		New York
University of Buffalo School of Medicine.....	(1929)		New York
Duke University School of Medicine.....	(1935)		Maryland
Ohio State University College of Medicine.....	(1921), (1937)		Ohio
University of Oklahoma School of Medicine (1933), (1934), (1935), (1936) Oklahoma			
Hahnemann Med. College and Hospital of Philadelphia (1936)			Penna.
Jefferson Medical College of Philadelphia.....	(1921)		Ohio
University of Pittsburgh School of Medicine.....	(1909)		Penna.
McHarg Medical College.....	(1937)		Tennessee
University of Tennessee College of Medicine.....	(1930)		Mississippi
(1928), (1936, 2), (1937, 2) Tennessee			
Vanderbilt University School of Medicine.....	(1913)		Illinois
(1933), (1937) Tennessee			

Baylor University College of Medicine.....	(1937)	Louisiana
Medical College of Virginia.....	(1937)	Virginia
University of Virginia Department of Medicine.....	(1932)	Virginia
Marquette University School of Medicine.....	(1913)	Wisconsin
McGill University Faculty of Medicine.....	(1935)	Washington
Schlesische-Friedrich-Wilhelms-Universität Medizinische Fakultät, Breslau	(1934)	New York
Ostcopathist Arkansas, Indiana, Iowa, 5, Kansas, Michigan, Missouri, Oklahoma, 5, South Dakota, Virginia		

School	LICENSED BY ENDORSEMENT	Year Endorsement Grad. of
University of Pennsylvania Department of Medicine....	(1898)	U. S. Army
* Examined in medicine and surgery.		
† License has not been issued.		
‡ Licensed to practice medicine and surgery.		

Book Notices

Industrial Surgery: Principles, Problems and Practice. By Willis W. Lasher, M.D., F.A.C.S., Assistant Professor of Traumatic Surgery, New York Post-Graduate Medical School, Columbia University, New York. Cloth. Price, \$6. Pp. 452, with 193 illustrations. New York: Paul B. Hoeber, Inc., 1938.

The wide scope in industrial surgery, which is only one department of industrial medical practice, is illustrated by the table of contents in this new work. The author states that there is scarcely a part of the human body which is not subject to the effects of trauma nor are there any tissues which have not become secondarily invaded by the complications associated with injury. Lasher's wide experience in industrial accidents serves as a basis for a comprehensive review of this field of surgery, with excellent chapters on general surgical considerations including a discussion of embryology, histology, physiology, biochemistry and surgical pathology. In developing his book the author has confined himself to his actual experiences and has not attempted to bridge over omissions by referring to other sources. In the preface the philosophy of industrial surgery is discussed and a sound approach to the various problems encountered is indicated which is well carried out throughout the text. The book includes chapters on the organization of medical departments in industry, an appendix describing various appliances used by the author, and a fairly complete bibliography. It should prove a valuable working manual in this field.

Endogene Endokrinotherapie in der Gynäkologie: Ätiologie und Behandlung des Karzinoms. Von Dr. Jules Samuels, Chirurg-Frauenarzt, Leiter der Einrichtung für Kurzwellentherapie, Amsterdam. Paper. Price, 4.90 florins. Pp. 182, with 32 illustrations. Leiden: A. W. Sijthoff's Uitgeversmaatschappij N. V., 1938.

During the last two years the author of this book has written three books and twenty-five articles, and the latter were published in Netherlands, German, French, British, American, Italian and Japanese journals. These books and articles dealt almost exclusively with one subject. The author devised an instrument which he calls a cycloscope, the essential part of which is a spectroscopic. He uses the instrument to study the endocrine glands and plots curves which he calls cyclograms. He makes many remarkable statements which have not as yet been substantiated by others. Some of these contentions are the following: Women ovulate two or three times a month and therefore can become pregnant this often during each intermenstrual interval. The author can tell by means of his instrument exactly which endocrine gland has a disturbed function and whether there is excessive or diminished hormonal activity of this gland. Likewise he can tell whether the dysfunction can be remedied or not. He can cure heretofore incurable endocrine disturbances by means of short wave therapy. He can successfully treat a dysfunctioning pituitary gland and in this way indirectly treat the mesencephalon and diencephalon. Duodenal and gastric ulcers have a central origin and the dysfunctioning of the stomach center is caused by a gonadotropic hyperpituitarism. Climacteric disturbances are due to dysfunctioning of the diencephalon under the influence of overproduction of gonadotropic hormone. The toxemias of pregnancy are due to hyperproduction of placental hormone, especially the placental estrogenic hormone. Many cases of genuine liver and kidney disease have a hormonal origin, which

consists of a hyperfunction of the gonadotropic hormones the result of a gonadotropic hyperpituitarism. Habitual abortion is due to hypoproduction of placental hormone, thereby enabling its antagonist, the posterior pituitary hormone, to act. Likewise hydatid moles have their origin in hypoproduction of placental estrogenic hormone. In cases of benign tumors there is always a gonadotropic hyperpituitarism and in cases of malignant tumors there is a thyrotropic hyperpituitarism. Therefore the endocrine electrodiagram is a helpful means of differentiating a benign from a malignant tumor. In the management of tumors, the pituitary must be treated. The most efficient way of treating carcinoma endocrinologically is to apply short wave therapy to the pituitary and to the gonads except in cases in which the gonads are already inactive. In such cases, treatment of the pituitary alone suffices. The author ends his book with the statement that the cycloscope is an indispensable instrument. However, thus far no one has published any confirmatory evidence in support of the author's contentions. In one large university in this country the cycloscope has failed completely to substantiate what Samuels claims for it.

The Synovial Membrane and the Synovial Fluid with Special Reference to Arthritis and Injuries of the Joints. By David H. Kling, M.D., Assistant Professor of Orthopedic Surgery and Chief of Arthritis Clinic, White Memorial Hospital, Los Angeles, California. Cloth. Price \$3. Pp. 229, with 80 illustrations. Los Angeles: Medical Press, 1938.

Few medical schools give instruction on the diagnostic and prognostic value of synovial fluid, in contrast to the emphasis placed on the cerebrospinal fluid. With the publication of Kling's readable monograph there is no longer any excuse for omitting consideration of the synovial fluid as actually and potentially as important as the spinal fluid. The present knowledge of the histogenesis, morphology and functions of the synovial membrane and its physiology are ably reviewed. The author has himself been one of the principal investigators in the field. Also the pathologic alterations of the synovial membrane in disease are discussed. This consideration of the synovial membrane is a necessary preliminary to accurate knowledge of the origin and function of synovial fluid and meaning of changes in this fluid as a reflection of the pathologic conditions. The monograph closes with four brief chapters on the clinical value of the aspiration of joint effusions and the technic and value of aspiration as a diagnostic procedure either alone or combined with injection of liquids and gases and their therapeutic usefulness. There are still many features of the synovial membrane and synovial fluid the exact significance of which is not yet determined. These holes in knowledge and interpretation are, however, rapidly filling, as can be determined by the number of recent references contained in the book. Furthermore the deficiencies in knowledge are not so large as to discourage the more widespread adoption of articular aspirations and further clinical pathologic studies. This monograph can be considered the most authoritative book in its field available today and it is hoped that the author will revise it at frequent intervals, since progress is so rapid that many of the hiatuses in knowledge may not remain unfilled for long.

Diseases of the Thyroid, Parathyroids and Thymus. By André Crotti, M.D., F.A.C.S., LL.D., Surgical Assistant at Roux's Clinic, Lausanne, Switzerland. Third edition. Leather. Price, \$20. Pp. 1,229, with 301 illustrations. Philadelphia: Lea & Febiger, 1938.

This edition closely resembles the previous edition in the luxuriousness of the makeup and the inevitable ribbon marker. The contents of the book have been enlarged by the addition of a chapter on the fundamental physiology and pathology of the parathyroid glands. The author freely injects his own ideas about the function of these glands and their various relationships to other organs and tissues of the body. Many of his conclusions are empirical and abrupt, presented in a staccato manner without sufficient discussion. Others are long and involved, fortified with case histories and reports of experimental studies; all statements seem overwhelmingly and equally positive. Endemic goiter is attributed to a fungus found in cabbage. The author cites some experimental proof of this according to his observations and claims to have fulfilled Koch's postulates. There is a great deal of information in this book which could have been

digested and presented in a much briefer content. The bibliography is complete but is presented at the back of the book without annotation, thus losing much of its value. The index is excellent, but the tyro in thyroid disease would soon lose himself in the maze. A research worker in thyroid disease would find this volume interesting if only because of the author's wide and long experience.

Health Education of the Public: A Practical Manual of Technic. By W. W. Bauer, B.S., M.D., Director, Bureau of Health and Public Instruction, American Medical Association, and Thomas G. Hull, Ph.D., Director, Scientific Exhibit, American Medical Association. Cloth. Price, \$2.50. Pp. 227, with 39 illustrations. Philadelphia & London: W. B. Saunders Company, 1937.

This practical manual of technic of health education of the public sets forth in detail the various means of health education at the disposal of the health officer, the medical society or the individual physician. It shows clear understanding of these methods and, while it explains them simply, they are discussed thoroughly. The authors first point out some of the sources of material for the health educator: books, magazines, health agencies, federal and local, and medical colleges and universities, with various lists of agencies where information can be obtained. The authors then evaluate the various means of disseminating this health information: the radio, the exhibit, the meeting, pamphlets, the newspaper, the motion picture, stereopticon slides, the magazine article, correspondence, books and miscellaneous devices, such as the healthmobile. They discuss each of these methods to determine how each of them can be used most effectively and they also give a list of subjects that may be used for timely talks. Every health educator should have a copy of this manual at hand for reference purposes.

Approved Laboratory Technic: Clinical, Pathological, Bacteriological, Mycological, Parasitological, Serological, Biochemical and Histological. By John A. Kolmer, M.D., Dr.P.H., Se.D., Professor of Medicine, Temple University, Philadelphia, and Fred Boerner, V.M.D., Assistant Professor of Bacteriology, School of Medicine and Graduate School of Medicine, University of Pennsylvania, Philadelphia. Second edition. Cloth. Price, \$8. Pp. 893, with 392 illustrations. New York & London: D. Appleton-Century Company, 1938.

As the title indicates, this edition was prepared under the auspices of the American Society of Clinical Pathologists. Each chapter has been revised and five new chapters have been added. These cover the subjects which have assumed importance in the seven years since publication of the first edition. Special emphasis is given to parasitology. The chapter on tissues also includes directions for the preparation of museum specimens. The most reliable methods and only those tests of approved value are given. The text is clear and concise; the procedures are definite and leave nothing to the imagination. Clinical pathologists, medical technicians and physicians performing laboratory tests will find this book not only a valuable one to own but the most reliable one to consult.

A Survey of Chronic Rheumatic Diseases Contributed by Contemporary Authorities in Commemoration of the Bicentenary of the Royal National Hospital for Rheumatic Diseases, Bath, 1738-1938. Compiled under the direction of the following Editorial Committee: R. G. Gordon, M.D., D.Sc., F.R.C.P., Chairman, G. P. R. Aldred-Brown, M.A., D.M., J. Barnes Burt, M.D., F. J. Poynton, M.D., F.R.C.P., R. Waterhouse, M.D., F.R.C.P., and G. D. Kersley, M.D., M.R.C.P., Secretary. Cloth. Price, \$6.50. Pp. 338, with illustrations. New York, Toronto & London: Oxford University Press, 1938.

This volume is issued to commemorate the bicentenary of the founding of the Royal Mineral Water Hospital at Bath. Its aim is to survey the current knowledge of rheumatic diseases. In pursuit of this purpose, recognized students of rheumatism from many lands have contributed chapters on different aspects of these diseases. Following a brief foreword reviewing some of the history of the Royal Mineral Water Hospital and its contributions to the country, especially in time of war, the book opens with a scholarly chapter on the history of chronic rheumatism by Sir Humphry Rolleston. While of necessity the discussion touches only the high spots, it serves as an excellent introduction to the subject. The French "concept of 'arthritisme'" is contributed in a chapter by Bezançon and Weil; a chapter on the osteo-arthritis syndrome by Polak of Paris is included. Professor Kahlmeter of Stockholm contributes an excellent chapter on the sedimentation rate in arthritis,

and Lindstedt of the same city on the pathogenesis and etiology of sciatica. The United States is ably represented in the excellent chapter by Hench on whether rheumatoid (atrophic) arthritis is a disease of microbic origin, one on the pathology of nonspecific arthritis by Ghormley, and chapters by Pemberton and Scull and by Osgood. Freund of Vienna has a chapter on the importance of biochemistry in the investigation of rheumatic diseases, and Aschoff of Freiburg on allergy in arthritis. Although most of the other chapters are, of course, written by eminent Englishmen, Van Dam of Amsterdam has one on radiography in rheumatism and the volume closes with one on organization and treatment of chronic rheumatism by Professor Van Breemen of Amsterdam. In spite of the multiplicity of authorship, the book is more than a collection of essays. It constitutes in its entirety a broad gage discussion of the present state of knowledge in many aspects of rheumatic diseases. No one, beginner or specialist, could fail to read it without obtaining much that is both informative and thought provoking.

Life and a Living: Report of the Committee for the Care of the Jewish Tuberculous, 1913-1936. Paper. Pp. 65, with illustrations. New York, [n. d.]

This report of the Committee for the Care of the Jewish Tuberculous deals with the care and rehabilitation of the tuberculous patient after graduation from the sanatorium. Through the Altro workshops, operated by the committee, the convalescent tuberculous person is given opportunity for paid employment. Easy jobs, light work or part time jobs are not always to be found. Employers still hesitate to place the ex-tuberculous among their apparently healthy employees for fear of infection. Hence the ex-tuberculous person finds it doubly hard to become self supporting. The aim of the Altro workshop as described in this report is to restore as far as possible the worker to his place in the community. This is not the only object of the rehabilitation program by this committee, as the committee points out that by its program it reduces materially the relapses among the patients discharged from the sanatorium. This booklet will be of value to the physician who has an interest in the problem of the ex-tuberculous in industry. Mention is made of similar projects in England, but no word is found of other like endeavors in this country.

Effect of Chronic Vitamin E Deficiency on the Nervous System and the Skeletal Musculature in Adult Rats: A Neurotropic Factor in Wheat Germ Oil. By Lårus Einarson, M.D., Professor of Anatomy, and Director of the Institute of Anatomy, University of Aarhus, Denmark, and Axel Ringsted, M.D., Assistant at the University Institute of Hygiene and the State Vitamin Laboratory, Copenhagen. Translated from Danish by Hans Andersen, M.D. Paper. Pp. 163, with 97 illustrations. Copenhagen: Levin & Munksgaard; London: Oxford University Press, 1938.

The first part of this monograph describes the clinical manifestations of neuropathic disturbances that develop in adult rats on a diet without vitamin E. These disturbances are prevented under certain conditions by a factor in wheat germ oil. The second part is devoted to a careful description of the extensive anatomic changes that may develop in the nervous system and skeletal muscles of adult rats fed without vitamin E. Whether the neurotropic principle in wheat germ oil is identical with vitamin E is not fully decided, but the facts at hand indicate that the two are identical.

The Chemistry of Antigens and Antibodies. By J. R. Marraek. Medical Research Council, Special Report Series, No. 230. Paper. Price, 3s. Pp. 194, with 27 illustrations. London: His Majesty's Stationery Office, 1938.

This report is a revised edition of report 194, published in 1935 under the same title. The usefulness of the earlier report indicated the need of revision in order to include the many important results of the work during the last few years on the chemistry of antigens and antibodies. The first chapter discusses such fundamental matters as the shapes and sizes of molecules, intermolecular (polar) forces, the structure of proteins and the stability of suspensions with special reference to antigen-antibody reactions. Then comes a consideration of the nature of antibodies, mainly from the point of view of their relation to proteins. The special topics considered are the

separation of antibodies from other serum constituents, the stability of antibodies, the antigen-antibody complex, the relation of antibody globulin to normal globulin, and the increase of serum proteins on immunization. The third chapter deals with the specificity of antigens, including artificial and natural protein antigens, polysaccharides and lipins. The last two chapters take up the nature of the antigen-antibody reaction, which is divided into two stages, specific combination and secondary reaction. At the end of each chapter is a list of appropriate references. There is a complete index. The first edition contained 135 pages. A work of great interest and usefulness to all students of pathogenic organisms and immunology has been brought well and thoroughly abreast of the times.

Actinomycosis. By Zachary Cope, B.A., M.D., M.S., Surgeon to St. Mary's Hospital, Paddington. Cloth. Price, \$5.50. Pp. 248, with 60 illustrations. New York, London & Toronto: Oxford University Press, 1938.

According to the author, this is the first monograph on actinomycosis in English. The first six chapters deal with general aspects of the disease: definition and history, characteristics of actinomyces, incidence, clinical features, diagnosis, prognosis and treatment. The history of the infection, the characteristics of the organism, the incidence, the general clinical features, the diagnosis, prognosis and treatment of the disease are considered as well as its localizations in different organs and tissues. There is a selected bibliography, an index of names and a subject index. Most of the illustrations are borrowed from older publications and many are now mainly of historical interest. Eight are in color. The monograph summarizes conveniently the knowledge of actinomycosis but it does not say anything about the disease that has not been said before.

Maternal Care Complications: The Principles of Management of Some Serious Complications Arising During the Antepartum, Intrapartum, and Postpartum Periods. Approved by the American Committee on Maternal Welfare, Inc. Prepared by R. D. Mussey, M.D., P. F. Williams, M.D., and F. H. Falls, M.D., F. L. Adair, M.D., Editor. Cloth. Price, \$1. Pp. 95. Chicago, Illinois: University of Chicago Press, 1938.

This booklet was written because of the enthusiastic response to the monograph which was published last year by the American Committee on Maternal Welfare, Inc., under the title "Maternal Care." The second volume presents the essential facts concerning the three major causes of maternal mortality, namely the toxemias of pregnancy, hemorrhages and puerperal infection. The three chapters were prepared by R. D. Mussey, P. F. Williams and F. H. Falls respectively. The second volume, like the first, should be carefully read and reread by every physician who practices obstetrics. If the general practitioners of this country were to learn the principles enumerated in this book and apply them to the best of their ability, there would be considerably less cause for worry about maternal and fetal death rates which exist at present. Every physician who cares for obstetric patients should possess a copy of this book.

An Introduction to Clinical Scotometry. By John N. Evans, M.D., F.A.C.S., Professor of Clinical Ophthalmology, Long Island College of Medicine. Published for Long Island College of Medicine. Cloth. Price, \$4. Pp. 266, with 57 illustrations. New Haven: Yale University Press, London: Oxford University Press, 1938.

This scientific monograph represents a compilation of study and material that the author has accumulated during the past nine years and is an effort to bring together the evidence from various sources so that it may be more available than in its present widely disseminated form in the periodical literature. In the fourteen main chapters he traces the history of plotting the central field of vision from the early part of the seventeenth century down to the present highly technical method of angioscotometry that he has developed and perfected. The necessary equipment, the technic, the application to clinical conditions and the theoretical considerations involved in central field work are described in sufficient but not unnecessary detail. There are enough illustrations to emphasize the desired points. The by-paths of angioscotometry are considered in the various appendices and to round it out there is a working bibliography of 320 references. As the name of Evans is intimately associated with angioscotometry, it must be stated emphatically that the book

is not given over to the highly scientific but clinically impractical plotting of the retinal vessels but deals rather with the clinical scotomas of the central visual field. Consequently the volume should have a definite place in the library of every modern ophthalmic clinician.

Structural Variations of the Human Iris and Their Heredity With Special Reference to the Frontal Boundary Layer. By Vilgo Eskeland, M.D. Paper. Price, 21s. Pp. 243, with illustrations. Copenhagen: Nyt Nordisk Forlag, Arnold Busck; London: H. K. Lewis & Co., Ltd., 1938.

This monograph deals with the structural variations of the iris and to a lesser extent the cornea. The author endeavors to classify the variations in his own inimitable manner, with a view to establishing the limit of the structural variations, their mutual relation and their frequency. The photographic examinations of the anterior surface of the iris were carried out on hundreds of patients and the endeavor was made to trace a hereditary relationship in the contour of the various aspects of the anterior iris. This was successful in only a limited percentage, corresponding to the earlier investigation of Weninger. Forty-four iris photographs, enlargements of Graflex prints, are reproduced. In the majority of instances the individual iris markings are badly blurred and this is increased by corneal reflex of the photo-flash lamp that was used for illumination. The photographs could not be called an unmitigated success. The last eighty-four pages of the monograph are devoted to an analysis of the patients, numbering well over 160. With each case is given the Bertillon-like formula of structure of the iris. However, the endeavor to classify human beings by the forms of the iris, similar to the classification by the form of the finger prints, is not a success. Neither is the relationship of iris structure sufficiently accurate to permit of recognition of paternity. The monograph is closed with a short bibliography. The enormous amount of work represented by this book must be available to interested research workers in libraries, but it is not worth a place in the library of a practical ophthalmologist.

The Pharmacological Shock Treatment of Schizophrenia. By Dr. Manfred Sakel. With a foreword by Professor Otto Pözl, Chief of the University Clinic for Neurology and Psychiatry of Vienna, Austria. Authorized translation by Joseph Wurtis, M.D., Research Fellow at the Bellevue Psychiatric Hospital of New York. Enlarged version of a series of articles from the Wiener medizinische Wochenschrift, 1934-35. Nervous and Mental Disease Monograph Series No. 62. Cloth. Price, \$2.15. Pp. 136, with illustrations. New York & Washington: Nervous and Mental Disease Publishing Company, 1938.

The book presents in convenient form Sakel's method of the insulin treatment of schizophrenia. The procedure is clearly outlined and many suggestions are made which will be helpful to the practitioner. Emphasis is laid on individualizing the procedure in different cases, but the criteria which decide at what phase the treatment should be interrupted are vague. A number of case histories are critically discussed. Sakel undoubtedly deserves credit for showing that schizophrenia can be "cured" by a treatment involving definite physiologic changes in the brain, but his attempts to account for them are unscientific. It seems to be regrettable that a book that is bound to be read by psychiatrists all over the country contains passages such as "The action of insulin therefore consists in: (1) neutralization of the excitant hormone and (2) vagotonic muffling of the cell." Investigations of other authors on the insulin treatment are almost completely omitted.

Surgical Handbook for Hospital Assistants in the Tropics. By W. K. Connell, M.B., Ch.B., F.R.C.S., Surgical Specialist, Tanganyika Territory. Cloth. Price, 12s. 6d. Pp. 440, with 177 illustrations. London: John Bale Medical Publications, 1938.

The problems presented in this book have no interest for medical practitioners in general. Army medical officers, especially in the tropics, might find this small volume instructive in the training of the orderly. The problems presented are peculiar to the British tropical service with its experience with native dispensers. Because of the quasimedical nature of its audience, presentation is dogmatic and brief. This is a dangerous policy, since duties seem to extend beyond first aid into the realm of diagnosis and treatment, which always require competent medical care.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Damages: Paralysis Following Cerebral Hemorrhage Mistaken for Drunkenness.—The plaintiff, a minister of the gospel, was a passenger on a bus operated by the Tri-State Transit Company. When the bus arrived at its destination the driver observed that the minister remained in his seat, apparently asleep, and attempted to arouse him. He was unable to do so and, thinking that the man was drunk, he called a helper and the two lifted the minister bodily from the seat in the bus, carried him into the waiting room of the station, put him in a chair, and left him. A short time thereafter, an outsider went into the waiting room and saw the minister lying prostrate on the floor. The ticket agent for the transit company, on being informed by this outsider of the supposed drunken condition of the minister, telephoned police headquarters stating that there was a drunken man at the station lying on the floor and asked that some one be sent to take charge of him. Two policemen who came in response to the call assumed, too, that the minister was drunk, carried him to police headquarters, entered a charge of drunkenness against him and locked him up. Apparently no further attention was paid to him until about twenty-four hours later, when the city physician was notified and immediately discovered that the minister had suffered a cerebral hemorrhage which had almost completely paralyzed him and rendered him speechless. A brother of the minister, summoned from a distance of about 100 miles, came and took charge of him. While at the time of the trial the minister's condition had considerably improved, he was still paralyzed and totally incapacitated. He brought suit against the Tri-State Transit Company and the Interurban Transportation Company for damages. The trial court's judgment for the defendants was affirmed by the court of appeals and the plaintiff appealed to the Supreme Court of Louisiana.

The Interurban Transportation Company was absolved from liability because the evidence showed that it had no contractual relationship with the plaintiff, who intended to continue his journey over that bus line but had purchased no ticket. The Supreme Court was of the opinion that the plaintiff had failed to make out his case against the remaining defendant, so far as he claimed damages for permanent and total disability. According to the testimony of physicians, it was not at all likely that medical attention, if administered immediately after the plaintiff suffered the stroke, would have averted the paralysis. In their opinion the paralysis which totally disabled the plaintiff would in any event have followed the stroke.

The assumption of the employees of the bus company that the plaintiff's limp and helpless condition was due to drunkenness, said the court, was extremely far fetched. But assuming that they did so believe and that they acted in good faith, their mistake was the misfortune of the company, and it is liable for injuries sustained by the plaintiff by reason of that mistake. After observing that a passenger is helpless and unable to take care of himself, from whatever cause, it is the duty of a carrier's employees to exercise reasonable care and diligence to make at least temporary provisions for his protection and comfort. A failure to do so is clearly a violation of the contract for safe passage. Instead of performing the duty in the present case, it was assumed without the slightest foundation, in the opinion of the court, that the plaintiff was in a drunken stupor and the report was spread abroad that he was drunk. Although the plaintiff was paralyzed and utterly helpless, he was not unconscious. He realized what was going on but could not explain or call for help. Not the slightest attention was paid to him during the time he lay in jail on the concrete floor. To say nothing of the pain and suffering resulting from the stroke, the suffering he must have undergone from the discomfort of lying on the floor without minis-

tration to his ordinary bodily needs, and the consciousness of his innocence and his utter inability to call for or to obtain help can well be imagined, the court said. He suffered some from the stroke itself. For this the carrier was not at fault. But the fact is that, if he had been afforded proper medical and other treatment, his discomfort and suffering would not have been so severe. For this item of damage, therefore, the court thought that the plaintiff should be awarded \$2,500.

As to the slander charge, there was no testimony that the plaintiff's reputation as a minister was injured. His friends and parishoners did not believe the report that he was drunk. But in the opinion of the court he was entitled to nominal damages for the false and slanderous charges made against him. The court assessed his damage under this item at \$1,000.

The judgments of the lower courts were therefore reversed and the Tri-State Transit Company was ordered to pay the plaintiff the sum of \$3,500.—*Scarey v. Interurban Transp. Co., Inc., et al. (La.), 179 So. 75.*

Workmen's Compensation Acts: Traumatic Aggravation of Perthes' Disease.—The employee, in the course of his employment, slipped on a greasy floor and fell, with legs spread apart, on to his right hip and the lower part of his back. An examination by the company physician, made three days later, disclosed no swelling or discoloration of the parts of the hip and back where the employee complained of pain. Several days later the company physician again examined him and discovered a limitation of motion of his right leg. A roentgenogram revealed that the head of the femur in the right hip was flattened. The employee was paid compensation for a period of eight months, after which it was discontinued. Thereafter, he instituted proceedings to recover additional compensation. The industrial commission denied the application, finding that the employee was suffering from chronic Perthes' disease and that this, not the accident, was the cause of his disability. The employee appealed to the Supreme Court of Minnesota, predicated his right to recover additional compensation on the theory that the accident had aggravated the pre-existing Perthes' disease.

Perthes' disease, said the Supreme Court, has been recognized only within comparatively recent years. It has its genesis in childhood while the femur is in a formative state. Whether it results from infection or from trauma is disputed; but its effect, whatever the cause, is the flattening of the head and the broadening of the neck of the femur. Since the head of the femur thereby becomes maladjusted to the socket into which it is supposed to fit, some limitation of the normal movement of the leg necessarily results. After the initial flattening and broadening of the femur occurs, the condition may remain quiescent for many years, but during adult life it has been noted in some cases that chronic or degenerative arthritis later develops. In its more advanced state it is accompanied by pain, muscle spasm in the vicinity of the affected bone, and considerable limitation of movement of the leg. It may originate without the knowledge of the afflicted person; its resurgent activity after a period of quiescence has been said to be due to traumatism caused by the overuse of a mechanically imperfect joint. It was conceded by the employee that the flattened and broadened condition of the femur existed at the time of the accident. He was then 43 years of age and had been employed at heavy manual labor all his life. He had never been sick and could remember no accident which might have caused Perthes' disease during his youth. He claimed that this accident aggravated the condition of his femur and that since the accident he had suffered pain and muscle spasm in the area of his right hip, had been unable to stand on his feet for any considerable period, that the movement of his leg was limited and a limp had developed through the shortening of the right leg, and that there had been atrophy of the muscles of his right thigh. The physicians of his selection who examined and treated him following the accident substantiated his contention.

The medical witnesses called by the employer and those appointed by the industrial commission categorically denied the truth of the employee's assertions. They testified that the

roentgenograms taken soon after the accident, when compared with those taken two years later, failed to show the slightest change in the abnormal condition of the femur and that therefore there was no justification for an assumption that the condition of the femur differed in the slightest from its condition at the time of the fall. They maintained that the accident imposed a strain on the soft parts of the body on which the relator fell without affecting the femur, and that the period for which compensation was paid was ample to permit a recovery from those strains to the soft tissue. They admitted that the condition of the femur would impose some limitation on the movement of the leg, but contended that this limitation at the time of the trial was no more extensive than it was when the accident occurred.

The court could find in the evidence nothing to justify it in overruling the findings of the commission and the order disallowing compensation was affirmed.—*Hens v. Armour & Co. (Minn.)*, 277 N. W. 923.

Accident Insurance: Death from Botulism as Death from "Bacterial Infection."—A life insurance policy containing a double indemnity clause provided that double indemnity was not payable if the insured's death resulted "from the taking of poison or . . . from any bacterial infection other than bacterial infection occurring in consequence of accidental and external bodily injury." It was admitted that the insured's death was due to botulism contracted through eating home-canned beans. The insurance company denied liability for double indemnity, contending that the death was due to "the taking of poison" or to "bacterial infection." The trial court gave judgment for the beneficiary, and the company appealed to the Supreme Court of Colorado.

Webster's New International Dictionary, said the court, defines infection to mean the "process of infecting" and the word "infect" to mean "to contaminate with a disease-producing substance, germs or bacteria." Technically, the court continued, the illness produced by bacteria themselves is referred to as infection, while that occasioned by the poison produced by such bacteria is referred to as poisoning. Gould's Dictionary of Medicine defines "botulism" as poisoning and defines "infection" as "the communication of disease-germs or virus by any means, direct or indirect." The same authority defines disease as "a condition of the body marked by inharmonious action of one or more of the various organs owing to abnormal condition or structural change." All of this, the court pointed out, merely reinforces and confirms the popular interpretation or commonly accepted meaning of bacterial infection as covering such afflictions as botulism, admittedly caused by the germ known as *Bacillus botulinus*. In the amended complaint the beneficiary contended "That said deceased on April 21, 1937, ate home canned beans containing *Bacillus botulinus* and then and there became infected with said bacillus." This statement was repeated in the stipulation of facts. The contentions, therefore, of the insurance company that death resulted from "bacterial infection" seemed to the court to be admitted by the beneficiary. Hence the exception contained in the insurance policy covered the case and the double indemnity clause was not applicable. The court, therefore, reversed the judgment of the trial court and remanded the case with instruction to enter judgment for the insurance company.—*New York Life Ins. Co. v. Moriano (Colo.)*, 76 P. (2d) 417.

Evidence: Right of Physician Witness to Testify Concerning Probable Effect of Injury.—In the trial of a personal injury suit in which it was alleged that the plaintiff's left leg was fractured when he was struck by a car driven by the defendant, a physician called by the plaintiff was asked the cause of the pain from which the plaintiff testified he suffered. The physician stated that in his opinion it was caused by adhesions that tended to limit the function of the limb; that is, fibrous unions between two tissues resulting from inflammation. The physician was then asked whether in his opinion the conditions caused by the adhesions were likely to be permanent. Basing his answer on his observations of the tendons and the condition of the leg, on his own knowledge and on the history of the

patient, the physician stated that the conditions were likely to be permanent and that with reasonable certainty the pain would continue permanently in the future. Another physician, who had taken roentgenograms of the plaintiff, when asked his opinion as to the cause of the pain in the region of the fractures after any sustained use of the leg, attributed it "to the atrophy of the muscles, to the shortening of both legs, to the angulation of the fragments and the change in the weight bearing line," which was impaired by reason of the bowing and angulation of the lower left leg. All this testimony was admitted over the objection of the defendant. From a judgment for the plaintiff the defendant appealed to the Supreme Court of Michigan.

The defendant contended that the testimony of the physician witnesses outlined above invaded the province of the jury and was therefore inadmissible. The Supreme Court, however, took a different view. A physician, said the court, may testify as to the extent of certain injuries, whether the injury is permanent or not, the probability of recovery, and the probable results of the injury. This, the court thought, did not come within the rule that excludes the opinion of a witness as to the ultimate fact that the jury is called on to determine. A medical man may testify as to his opinions concerning the condition of the human system, the probability of recovery from an injury and other matters peculiarly within his professional knowledge. When the court or jury can make its own deductions, deductions may not be made by witnesses. In this case the probable effects of an injury such as that suffered by the plaintiff could be shown only by the opinion of a competent physician. The physicians testified fully as to the facts on which they based their conclusions and were entitled to give their opinions on the probable effect of the injury that the plaintiff received. For the reasons stated, and others not here pertinent, judgment in favor of the plaintiff was affirmed.—*Pearce v. Rodell (Mich.)*, 276 N. W. 883.

Society Proceedings

COMING MEETINGS

- Academy of Physical Medicine, Washington, D. C., Oct. 24-26. Dr. Herman A. Osgood, 144 Commonwealth Ave., Boston, Secretary.
- American Academy of Ophthalmology and Oto-Laryngology, Washington, D. C., Oct. 9-14. Dr. William P. Wherry, 107 South 17th St., Omaha, Executive Secretary.
- American College of Surgeons, New York, Oct. 17-21. Dr. George W. Crile, 40 East Erie Street, Chicago, Chairman, Board of Regents.
- American Public Health Association, Kansas City, Mo., Oct. 25-28. Dr. Reginald M. Atwater, 50 West 50th St., New York, Executive Secretary.
- American Society of Tropical Medicine, Oklahoma City, Nov. 15-18. Dr. E. Harold Hinman, Wilson Dam, Ala., Secretary.
- Associated Anesthetists of the United States and Canada, New York, Oct. 17-21. Dr. F. H. McMechan, 318 Hotel Westlake, Rocky River, Ohio, Secretary General.
- Association of American Medical Colleges, Syracuse, N. Y., Oct. 24-26. Dr. Fred C. Zapffe, 5 South Wabash Ave., Chicago, Secretary.
- Association of Military Surgeons of the United States, Rochester, Minn., Oct. 13-15. Dr. H. L. Gilchrist, Army Medical Museum, Washington, D. C., Secretary.
- Central Association of Obstetricians and Gynecologists, Minneapolis, Oct. 6-8. Dr. William F. Mengert, University Hospitals, Iowa City, Secretary.
- Central Society for Clinical Research, Chicago, Nov. 4-5. Dr. Lawrence D. Thompson, 4932 Maryland Ave., St. Louis, Secretary.
- Clinical Orthopedic Society, Nashville, Tenn., and Birmingham, Ala., Oct. 7-8. Dr. H. Earle Conwell, 215 Medical Arts Bldg., Birmingham, Ala., Secretary.
- Delaware, Medical Society of, Dover, Oct. 10-12. Dr. Allan V. Gilliland, Smyrna, Secretary.
- Indiana State Medical Association, Indianapolis, Oct. 4-6. Mr. Thomas A. Hendricks, 23 East Ohio St., Indianapolis, Executive Secretary.
- Inter-State Postgraduate Medical Association of North America, Philadelphia, Oct. 31-Nov. 4. Dr. W. B. Peck, 27 East Stephenson St., Freeport, Ill., Managing Director.
- Kentucky State Medical Association, Louisville, Oct. 3-6. Dr. Arthur T. McCormack, 620 South Third St., Louisville, Secretary.
- Omaha Mid-West Clinical Society, Omaha, Oct. 24-28. Dr. J. D. McCarthy, 107 South 17th St., Omaha, Secretary.
- Pacific Association of Railway Surgeons, Los Angeles, Oct. 7-8. Dr. W. T. Cummins, Southern Pacific General Hospital, San Francisco, Secretary.
- Pennsylvania, Medical Society of the State of, Scranton, Oct. 3-6. Dr. Walter F. Donaldson, 500 Penn Ave., Pittsburgh, Secretary.
- Southern Medical Association, Oklahoma City, Nov. 15-18. Mr. C. P. Loranz, Empire Bldg., Birmingham, Ala., Secretary.
- Southwestern Medical Association, El Paso, Texas, Nov. 3-5. Dr. Orville E. Egbert, 116 Mills St., El Paso, Texas, Secretary.
- Vermont State Medical Society, Burlington, Oct. 6-7. Dr. B. F. Cook, 154 Bellevue Ave., Rutland, Secretary.
- Virginia, Medical Society of, Danville, Oct. 4-6. Miss Agnes V. Edwards, 1200 East Clay St., Richmond, Secretary.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1928 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but may be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American Journal of Medical Sciences, Philadelphia

196:153-304 (Aug.) 1938

United States Army's War in the Air Against the Mosquito-Borne Diseases. J. S. Simmons, Boston.—p. 153.

*Statistical Study of Acute Hemorrhagic Pancreatitis (Hemorrhagic Necrosis of Pancreas). H. A. Weiner and R. Tennant, New Haven, Conn.—p. 167.

Nature and Mechanism of Staining of Erythrocytic Reticulum. S. Nittis, Ann Arbor, Mich.—p. 177.

Acute Hemolytic Anemia. H. M. Greenwald, Brooklyn.—p. 179.

Observations on Etiology of Toxemias of Pregnancy: V. Etiologic Relationship Between Water Retention and Arterial Hypertension. M. B. Strauss, Boston.—p. 188.

Observations on Referred Pain of Cardiac Origin. S. Robertson and L. N. Katz, Chicago.—p. 199.

Paradoxical Embolism. D. W. Ingham, Rochester, Minn.—p. 201.

Radiologic Measurements of the Apical Basal Relaxation of the Lung During Artificial Pneumoperitoneum Treatment. A. L. Banyai, Wauwatosa, Wis.—p. 207.

Diabetic Coma Requiring an Unprecedented Amount of Insulin: Report of Case Manifesting Extreme Insulin Resistance. H. J. Wiener, New York.—p. 211.

Hyperinsulinism and Pregnancy: Report of Case. E. B. LeWinn, Philadelphia.—p. 217.

Uveoparotid Fever (Heerfordt's Syndrome): Neurologic Manifestations: Report of Two Cases. D. Arhuse and M. Madonick, New York.—p. 222.

Regeneration of Adrenal Gland Following Enucleation. D. J. Ingle and G. M. Higgins, Rochester, Minn.—p. 232.

Effects of Pressor Substance Obtained from Kidneys on the Renal Circulation of Rats and Dogs. A. Merrill, Atlanta, Ga.; R. H. Williams and T. R. Harrison, Nashville, Tenn.—p. 240.

Typhus Fever in Pennsylvania. H. F. Flippin, Philadelphia.—p. 246.

Disease and the Negro. G. Walsh and R. M. Pool, Fairfield, Ala.—p. 252.

Relationship of Orthopedic Surgery to Internal Medicine. H. T. Hyman, Long Branch, N. J.—p. 261.

*Effect of Prontosil and Related Compounds on Chemotropism of Leukocytes. D. R. Coman, Philadelphia.—p. 273.

Acute Hemorrhagic Pancreatitis.—The belief that alcohol is in some way related to acute hemorrhagic pancreatitis has developed in the department of pathology of the New Haven Hospital from a review of the clinical histories of fatal cases of this disease. This has been fortified by a not infrequent case with an explosive clinical course and striking postmortem observations, in the light of which Weiner and Tennant undertook an analysis of 4,000 necropsies. Each anatomic diagnosis was reviewed and all protocols in any way related to pancreatic disease were abstracted, with especial emphasis on the clinical history (including alcoholism), the chief anatomic causes of death and also the postmortem condition of the stomach, pancreas, liver and gallbladder. All the available slides of liver and pancreas in these cases were reviewed. There were thirty-eight instances of acute hemorrhagic pancreatitis and ninety-seven of chronic pancreatitis. In twenty-five of the acute cases, alcohol was an associated factor. In six, disease of the extrahepatic biliary tract was present. Of fifty-one persons dying during acute alcoholic episodes, twenty-seven had pancreatic lesions (twenty-five acute and two chronic). In forty-one instances of chronic alcoholism nineteen showed pancreatic lesions, all of a chronic nature. In fifty-one instances of periportal cirrhosis, twenty-five showed pancreatic lesions. In 343 cases of disease of the extrahepatic biliary tract there were six instances of acute pancreatitis and twenty-one of chronic pancreatitis. While the data offer no relation to the pathogenesis of acute pancreatitis, they indicate at least the complexity of the problem. The results show an increase of from forty to fifty times in the incidence of pancreatic disease when a history of alcoholism exists.

Sulfanilamide Compounds and Chemotropism of Leukocytes.—Coman conducted experiments using a sulfanilamide compound (Prontosil-Losung, Bayer) absorbed on kaolin, carbon and streptococci in an attempt to determine the chemotropic effect of the drug for polymorphonuclear leukocytes. Leukocytes were obtained from the peritoneal cavity of rabbits. Although the prontosil slightly reduced the negatively chemotropic effect of kaolin, it did not cause a positive chemotropic response. Adsorbed to carbon and to streptococci, the prontosil did not alter the directional movement of the leukocytes in relation to the adsorbing agents. There is, then, no evidence from these experiments that prontosil attracts leukocytes. Experiments in which sulfanilamide (Merck) was used as the attracting substance showed that this substance exerted a toxic effect on the leukocytes which was expressed in a cessation of their movements. Experiments in which a benzoyl derivative of sulfanilamide (setazinc, Merck) was used as the source of attraction showed that this substance exerted only a weak attraction for the leukocytes and this was not constant. It seems unlikely from these experiments that the therapeutic action of these drugs is due to an increased chemotropism of polymorphonuclear leukocytes.

American Journal of Orthopsychiatry, Menasha, Wis.

S: 409-584 (July) 1938

Enuresis: A Method for Its Study and Treatment. O. H. Mowrer and Willie Mae Mowrer, New Haven, Conn.—p. 436.

Incidence of Enuresis and Age of Cessation in 100 Delinquents and 100 Sibling Controls. J. J. Michaels, Boston.—p. 460.

Clinical Experience with Play Therapy. M. Gitelson and collaborators, Chicago.—p. 466.

Active Play Therapy. J. C. Solomon, Baltimore.—p. 479.

Archives of Internal Medicine, Chicago

62:181-354 (Aug.) 1938

*Culture of Human Marrow: Comparative Study of the Effects of Sulfanilamide and Antipneumococcus Serum on the Course of Experimental Pneumococcal Infections. E. E. Osgood, with technical assistance of Inez E. Brownlee, Portland, Ore.—p. 181.

Hyperparathyroidism Due to Idiopathic Hypertrophy (Hyperplasia?) of Parathyroid Tissue: Follow-Up Report of Six Cases. F. Albright, H. W. Sulkowitch and E. Bloomberg, Boston.—p. 199.

Removal of Intravenously Injected Bromsulphalein from the Blood Stream of the Dog: Comparison of the Removal of Intravenously Injected Bilirubin and That of Bromsulphalein. M. A. Mills and C. A. Dragstedt, Chicago.—p. 216.

Excretion of Bile Pigment and Hepatic Function in Diseases of the Blood. W. H. Barker, Baltimore.—p. 222.

*Experimental Streptococcal Endocarditis. R. A. Kinsella and R. O. Muether, St. Louis.—p. 247.

Lesions of Peripheral Nerves in Thrombo-Angiitis Obliterans: Clinicopathologic Study. N. W. Barker, Rochester, Minn.—p. 271.

Boeck's Sarcoid: Report of Case, with Clinical Diagnosis Confirmed at Autopsy. J. Spencer and S. Warren, Boston.—p. 285.

*Oral Ragweed Pollen Therapy: Clinical Results of Experiments on Gastrointestinal Absorption. T. B. Bernstein and S. M. Feinberg, Chicago.—p. 297.

Infectious Diseases: Review of Current Literature. H. A. Reimann, Philadelphia.—p. 305.

Culture of Human Marrow.—Osgood found by studying cultures of human marrow that sulfanilamide exhibits a slight bacteriostatic action on pneumococcal infections which is increased by an increase in concentration. Even 0.3 unit per cubic centimeter of specific antipneumococcus serum is more effective against the type I pneumococcus than is sulfanilamide alone. Sulfanilamide plus any given dose of antiserum less than the amount which will by itself reduce colony counts to nearly zero is more effective than corresponding doses of antiserum alone. The results support the view that sulfanilamide renders the organism more vulnerable to bactericidal substances present in the serum: If the results of these in vitro experiments are applicable to infections in human beings, sulfanilamide therapy should be of value in pneumococcal pneumonia and might delay death in pneumococcal meningitis, but alone it will not prove as effective as even small amounts of type-specific antiserum. If used in conjunction with antiserum it should further lower the mortality with the present doses of antiserum or should give an equally low mortality with smaller doses of antiserum.

Experimental Streptococcal Endocarditis.—Kinsella and Muether injured the mitral valve or the chordae tendineae of seventeen dogs and then fed them living cultures of non-

hemolytic streptococci either mixed with food or by stomach tube. Ten of the animals became sick, displayed positive results of blood culture and died. At necropsy these infected animals had bacterial endocarditis. The bacteria in the vegetations were found to be identical with those that had been fed to the animals. Bacteria entering the animal body through the mouth may become implanted on an injured area within the body. The exact route which these bacteria follow is not determined.

Oral Ragweed Pollen Therapy.—Bernstein and Feinberg gave extract of ragweed pollen to twenty patients allergic to ragweed. The duration of treatment was from one to three weeks. In determining the strength of the initial doses the relation of the oral to the hypodermic dose was kept in mind. One drop of a 1:33 extract of ragweed pollen was regarded as a probably safe initial dose, since it is about 450 times the strength of the first dose (0.05 cc. of a 1:10,000 extract) usually given hypodermically. The doses were given three times daily well diluted. In most instances the maximal dose was from 10 to 15 drops at the end of a week. In two cases a maximal dose of 30 drops was used. No benefit whatever was experienced by eighteen patients with regard to the symptoms of hay fever and asthma. Two obtained moderate improvement, in one of whom while there was some improvement in the hay fever there was no improvement in the asthma. In other words, there was no amelioration of the asthma in any instance. In six patients the pollen extract caused gastrointestinal disturbances, consisting mainly of colicky abdominal pain and nausea.

Archives of Neurology and Psychiatry, Chicago

40: 227-416 (Aug.) 1938

- *Biopsy Studies of Cerebral Pathologic Changes in Schizophrenia and Manic-Depressive Psychosis. A. R. Elvidge and G. E. Reed, Montreal.—p. 227.
- Sweat Secretion in Man: III. Clinical Observations on Sweating Produced by Pilocarpine and Mecholyl. C. F. List and M. M. Peet, Ann Arbor, Mich.—p. 269.
- Intracerebral Blood Flow: Experimental Study. N. C. Norcross, Philadelphia.—p. 291.
- *Mechanism of After-Contraction: Further Studies. M. R. Sapirstein, R. C. Herman and I. S. Wechsler, New York.—p. 300.
- Intercellular Substance of the Cerebral Cortex (Nissl's Cerebral Gray Matter): Physiologic Significance. A. E. Taft, Philadelphia.—p. 313.
- Moro Reflex and Startle Pattern. K. Goldstein, C. Landis, W. A. Hunt and F. M. Clarke, New York.—p. 322.
- Arnold-Chiari Malformation and Its Operative Treatment. W. Penfield and D. F. Coburn, Montreal.—p. 328.
- Distribution of Affected Nerve Cells in a Case of Amyotonia Congenita. J. L. Conel, Boston.—p. 337.
- Thalamic Dysfunction: Report of Case in Which a Thalamic Syndrome Was Treated by Excision of a Porencephalic Cyst. H. L. Kozol, Boston.—p. 352.

Cerebral Changes in Psychosis.—Elvidge and Reed obtained twenty-six specimens of cerebral tissue for biopsy from nineteen psychotic patients between 20 and 40 years of age; thirteen with schizophrenia, five with manic-depressive psychosis and one with so-called toxic encephalitis. A second operation was performed on seven of the patients at the end of from one to two years, and thus useful data were furnished as a control. Sixteen specimens serving as controls were taken from routine surgical material with a similar or an identical technic. Swelling of the oligodendroglia cells occurred in association with schizophrenia and manic-depressive psychosis. There was often accompanying mild hypertrophy of the astrocytes. Two main types of oligodendroglial change were observed: that in which the nuclei were normal and that in which they were pyknotic. Swelling of oligodendroglia cells was observed in two patients with status epilepticus who were mentally confused between seizures. It existed in one patient at the time of an epileptic seizure. The change in the oligodendroglia cells in psychotic patients occurred in the white matter. It may be general or patchy in distribution. At a depth of 1 cm. and in the deeper layers it was often more intense. In view of the changes in the oligodendroglia cells, it is suggested that the mental phenomena are associated with massive physiologic disturbances in associational and commissural fibrous pathways in the brain. In this way impulses from different parts of the brain are interrupted, with consequent disturbance and loss of control in the intellectual, volitional and

emotional fields. By analogy with the other states in which swelling of oligodendroglia cells is observed, it is justifiable to assume that in psychotic states also there may be a causal toxic or metabolic factor.

After-Contraction.—How far one may utilize the concept of after-contraction in studies of ordinary motor learning Sapirstein and his collaborators do not say, but for the production of after-contraction a large initial stimulus produced by external forces is not necessary. Supporting the weight of the limb itself is sufficient. In walking or running there is a repetitive movement, perfectly coordinated, which eventually is made with almost no conscious effort; indeed, the movement seems entirely automatic. It is easily believable that a basic factor involved here is that represented by after-contraction, which is a sustained cortical excitatory state responding in a rhythmic fashion to stimuli of which the subject is unconscious. Physiologically, after-contraction is influenced by facilitation, fatigue and changes in initial load and duration of effort. The phenomenon is always reenforced by simultaneous contraction of ipsilateral muscles and is frequently inhibited by contraction of contralateral muscles. A relatively normal reaction is associated with tabes and cerebellar syndromes, a prolonged after-contraction with paralysis agitans and a diminished response with disease of the pyramidal tracts. After-contraction is mainly an after-discharge from the cortex or its projection pathways. It is modified by other parts of the nervous system, as is voluntary activity. Suggestions are offered concerning the usefulness of after-contraction as a method of investigating the physiologic behavior of the cortex and of studying drugs used in controlling its excitability. Theoretical views are advanced as to the possible role of after-contraction in habit formation.

Archives of Ophthalmology, Chicago

20: 175-358 (Aug.) 1938

- Disturbances of Vertical Motor Muscles of the Eyes. A. Bielschowsky, Hanover, N. H.—p. 175.
- Perimetric Studies in Syphilitic Optic Neuropathies. Louise L. Sloan and A. C. Woods, Baltimore.—p. 201.
- Cancer of the Eyelids, Conjunctiva and Cornea: II. Squamous Cell Epithelioma. H. L. Birge, Rochester, Minn.—p. 254.
- *Treatment of Staphylococcal Conjunctivitis with Staphylococcus Toxoid: Preliminary Note. P. Thygeson, New York.—p. 271.
- Mannitol Fermentation as Indicator of Conjunctival Pathogenicity of Staphylococci. P. Thygeson, New York.—p. 274.
- Recurrent Retinal and Vitreous Hemorrhages in the Young—Eales' Disease: Report of Two Cases. R. T. Paton, New York.—p. 276.
- An Ophthalmic Carriage. J. N. Evans, Brooklyn.—p. 286.
- Topography and Frequency of Complications of Uveal Sarcoma. B. Kronenberg, New York.—p. 290.
- Inositol in Ocular Tissues. A. C. Krause and R. Weekers, Chicago.—p. 299.
- Detachment of the Retina: Summary of Modern Opinions. T. D. Allen, Chicago.—p. 307.

Staphylococcal Conjunctivitis.—In view of the efficacy of immunization with staphylococcus toxin in protecting rabbits against instillations of toxin which would produce severe conjunctivitis in normal rabbits, Thygeson attempted to obtain healing in fifty-seven human beings with conjunctivitis by immunization with toxoid. Only persons were chosen whose conjunctivitis had resisted local treatment for not less than two months. The majority of the patients had had conjunctivitis for more than a year. The toxoid was given biweekly, starting with an initial injection of 0.01 cc. of dilution. 2. The dose was increased to a maximum of 1 cc. in steps of 0.02, 0.04, 0.06, 0.08, 0.1, 0.2, 0.4, 0.6 and 0.8 cc. Injections of less than 0.5 cc. were given intradermally and the remainder were given subcutaneously. In cases in which noticeable improvement did not occur on completion of the series, injections of 0.5 cc. were continued at weekly intervals for at least six weeks. Healing occurred in twenty-one of the fifty-seven patients, nineteen showed clinical improvement and the condition of seventeen remained unchanged. The cultures of twenty-four of the fifty-seven patients became negative. There was a recurrence of symptoms after periods varying from four to six months in eight of the persons in whom clinical healing occurred. In all these the symptoms disappeared after a second course of toxoid therapy. This recurrence was probably related to the fact that in seven of the eight patients

some toxigenic staphylococci were still present after healing. The cultures of the thirteen patients in whom healing occurred, and who have as yet had no recurrence, were negative after healing. The results obtained warrant further clinical trial of staphylococcus toxoid.

Florida Medical Association Journal, Jacksonville

25: 53-104 (Aug.) 1938

- Ectopic Pregnancy. L. J. Netto, West Palm Beach.—p. 65.
Therapy in Modern Psychiatry. W. G. Miles, Chhattahoochee.—p. 71.
Gonococcal Peritonitis of the Upper Right Quadrant. T. F. Hahn, De Land.—p. 73.
Cooperation of Railroad Surgeons. W. J. Lancaster, Wilmington, N. C.—p. 75.
Relief of Pain by Intraspinal (Subarachnoid) Injection of Alcohol. C. S. Franckle, St. Petersburg.—p. 80.

Iowa State Medical Society Journal, Des Moines

28: 373-420 (Aug.) 1938

- Diseases Associated with Characteristic Changes in the Red Blood Cells: Microcytic and Macrocytic Anemias. C. C. Sturgis, Ann Arbor, Mich.—p. 373.
Regional Enteritis. J. V. Prouty, Cedar Rapids.—p. 379.
Management of Uterine Malignancy. R. F. Martin, Sioux City.—p. 382.
Prevention of Poliomyelitis. F. Moore, Des Moines.—p. 385.
*Delayed Resolution in Bronchopneumonia. F. N. Cole, Iowa Falls.—p. 389.
Manifestations of Insulin Hypoglycemia Mistaken for Other Disease in Patients with Known Diabetes Mellitus. W. L. Randall, Hampton, A. E. Feller and J. A. Greene, Iowa City.—p. 392.

Delayed Resolution in Bronchopneumonia.—In considering the problem of delayed resolution in bronchopneumonia it seems likely to Cole that one is not dealing with a true pathologic entity but with a variety of conditions. There is a definite need for more clinical investigation under controlled conditions. Many cases of this nature are seen in the home in which facilities for careful diagnostic studies are lacking. Under ideal conditions, one should have serial roentgenograms in every case of bronchopneumonia. Bronchoscopic examination should be made of those patients who fail to recover promptly. It may be found that so-called nonresolution is really due to localized areas of atelectasis or to occlusion of a bronchus or a bronchiole. Treatment is bound to be empiric until the condition is better understood.

Journal of Thoracic Surgery, St. Louis

7: 575-690 (Aug.) 1938

- Extrapleural Pneumothorax. R. Belsey, London, England.—p. 575.
*Extrapleural Pneumothorax in Treatment of Pulmonary Tuberculosis: Preliminary Report. R. H. Overholt, Boston, and O. S. Tubbs, London, England.—p. 591.
Resection of Thoracic Esophagus: Clinical and Experimental Study. W. E. Adams, L. Escudero, H. G. Aronsohn and M. M. Shaw, Chicago.—p. 605.
Carcinoma of Lower Thoracic Esophagus: Report of Successful Resection and Esophagogastronomy. W. E. Adams and D. B. Phenister, Chicago.—p. 621.
Upper Esophagotomy: Its Indications and Uses. C. Eggers, New York.—p. 633.
Role of Dual Pulmonary Circulation in Various Pathologic Conditions of the Lungs. D. A. Wood and Miriam Miller, San Francisco.—p. 649.
Observations on Sources of Pulmonary Hemorrhage and Attempts at Its Control. L. Eloesser, San Francisco.—p. 671.

Extrapleural Pneumothorax in Pulmonary Tuberculosis.—Up to the present Overholt and Tubbs selected only those patients for extrapleural pneumothorax for whom any other form of collapse therapy offered no hope of a successful outcome. Extrapleural pneumothorax is not introduced to replace the modern selective thoracoplasty but is an alternative measure when the latter is contraindicated. The factors which render the patient with pulmonary tuberculosis unsuitable for thoracoplasty are evidence of too great activity, extensive bilateral lesions of a fibrocavernous nature and complicating factors (insufficient cardiovascular reserve, generalized emphysema, asthma and the like). The operation has been performed thirty-one times (in twenty-eight patients) under cyclopropane and oxygen inhalation anesthesia or a combination of local infiltration with paravertebral block of the upper intercostal nerves, 1 per cent procaine hydrochloride being used. On return to the ward, an oxygen tent has rarely been needed even in the bad risk patients. Intravenous infusion has been used if the blood pressure fell below 100 systolic, so that the patient may

sit up soon after operation. All the patients had more or less interstitial emphysema during the first twenty-four hours, but in no case has it caused any distress other than slight tenderness of the affected tissues. Sputum was not retained for more than thirty-six hours. Following pneumolysis, patients are able to expectorate more efficiently and sooner than after thoracoplasty. The frequency and amount of air refills to maintain the space so as to give the desired selective collapse have been controlled by frequent roentgenograms, fluoroscopy and consideration of the manometric pressures. In three cases almost the whole space became filled with blood clots which could not be aspirated through a needle. Infection in the extrapleural space developed in four patients. In three of these there is definite evidence of a bronchial fistula. In another case evidence is lacking, although it is possible that the lateral wall of the cavity became necrotic because of its separation from the wall of the chest. Regardless of this complication, the patient has improved sufficiently to consider thoracoplasty. The authors believe that most of the patients will eventually require conversion of the extrapleural pneumothorax to the permanent collapse of thoracoplasty. This prediction is made because of the extensive disease present in those selected for this form of treatment. Should the operation eventually be applied more widely to include young patients with less extensive disease, the ultimate fate of the space would be subject to the same rules that apply to an intrapleural pneumothorax.

Kentucky Medical Journal, Bowling Green

26: 301-348 (Aug.) 1938

- Practical Diagnosis and Treatment of the Acute Abdomen. L. R. Ellars, Louisville.—p. 303.
Common Errors in the Diagnosis of Hyperthyroidism. A. E. Grimes, Lexington.—p. 307.
The Physiology of Edema Formation. H. Lawson, Louisville.—p. 309.
Disease Masquerades in Heart Symptoms. E. F. Horine, Louisville.—p. 313.
Intussusception in Infancy and Childhood. G. P. Grigsby and S. E. Kaplan, Louisville.—p. 318.
Agranulocytosis. J. Stites and F. M. Stites, Louisville.—p. 324.
Anesthesia. D. M. Dollar, Louisville.—p. 328.
Study of Maternal Deaths, Infant Deaths and Cesarean Sections in the Louisville Kentucky Hospitals. W. T. McConnell, Louisville.—p. 336.
Postural Treatment of Pulmonary Tuberculosis. B. L. Brock and T. A. Woodson, Louisville.—p. 343.

Maine Medical Journal, Portland

29: 161-180 (Aug.) 1938

- Low Transverse Cervical Cesarean Section. A. P. Leighton, Portland.—p. 161.
Mortality in Surgical Diabetes in the General Hospital: Medical Study of 100 Operated Cases. E. R. Blaisdell, Portland.—p. 165.
Infectious Mononucleosis (Glandular Fever): Report of Case Presenting Symptoms of Acute Appendicitis. R. A. Beliveau and B. W. Russell, Lewiston.—p. 167.

Missouri State Medical Assn. Journal, St. Louis

33: 299-342 (Aug.) 1938

- Menstruation and Dysmenorrhea. W. B. Brown, Columbia.—p. 299.
Present Day Therapy of Varicose Veins. C. K. Higgins, St. Louis.—p. 305.
Intussusception with Procidencia Through an Ulcerated Ventral Hernia: Report of Case. H. F. Burkwall, Kansas City.—p. 308.
Early Symptoms of Genito-Urinary Disease. H. M. Young, Columbia.—p. 310.
Roentgenologist Looks at Gastric Cancer. S. A. Levey, St. Louis.—p. 316.
Practical Method of Blood Transfusion in the Home. J. H. Keim, Kennett.—p. 320.
The Future of Thyroid Surgery. W. Bartlett, St. Louis.—p. 322.

Nebraska State Medical Journal, Lincoln

23: 281-320 (Aug.) 1938

- Immunologic Aspects of Syphilis. C. C. Dennie, Kansas City, Kan.—p. 281.
Nebraska's Program of Venereal Disease Control. E. G. Zimmerer, Lincoln.—p. 286.
Treatment of Acute and Subacute Gonorrhea. W. J. McMartin, Omaha.—p. 289.
Early Syphilis and Its Cutaneous Manifestations. C. C. Tomlinson, Omaha.—p. 292.
Prevention and Treatment of Neurosyphilis: Results in Seventy-Two Cases of Asymptomatic and Clinical Neurosyphilis by Combined Artificial Fever and Chemotherapy. A. E. Bennett and M. D. Lewis, Omaha.—p. 295.
Cardiovascular Disease. J. C. Thompson, Lincoln.—p. 301.
Fever Therapy in Treatment of Gonorrhea. C. A. Owens, Omaha.—p. 308.

Northwest Medicine, Seattle

37: 231-270 (Aug.) 1938

- Chronic Cicatricial Obstruction of Extrahepatic Bile Ducts. C. E. Hagyard, Seattle.—p. 237.
 Primary Pyocyanous Meningitis: Report of Case Ending in Recovery. E. H. Berger, Portland, Ore.—p. 242.
 Residual Abscesses After Ruptured Appendicitis. M. S. Rosenblatt, Portland, Ore.—p. 245.
 Modern Rationale in the Treatment of Pneumonia. H. J. Friedman, Seattle.—p. 246.
 Improved Method of Administering Oxygen by Nasal Catheter. T. W. Houk, Seattle.—p. 248.
 Public Health Aspects of Pneumonia. D. G. Evans, Seattle.—p. 250.
 Inexpensive Watch Glass Museum Mountings: Improved Technic. C. P. Larson, Fort Steilacoom, Wash., and E. J. Levin, Tacoma, Wash.—p. 254.

Ohio State Medical Journal, Columbus

34: 841-960 (Aug.) 1938

- Bilateral Nephrolithiasis and Ureterolithiasis. I. Abell, Louisville, Ky.—p. 857.
 Self Selection of Diet Experiment: Its Significance for Feeding in the Home. Clara M. Davis, Winnetka, Ill.—p. 862.
 Spontaneous Hypoglycemia Associated with Pancreatic Adenoma: Case Report with Operation and Autopsy. L. A. Levison and T. L. Ramsey, Toledo.—p. 869.
 Management of Burns of the Cornea. A. M. Culler, Dayton.—p. 873.
 Hypophylid Cachexia (Simmonds' Disease): Report of Two Cases with Autopsy Findings. M. A. Davis, Painesville, and Beatrice Bostle, Columbus.—p. 879.
 Acute Intestinal Obstruction. B. H. Nichols, Cleveland.—p. 884.
 Place of the Hospital in Maternal Welfare. P. F. Williams, Philadelphia.—p. 887.
 Poliomyelitis: Symptomatology and Treatment: Part II. F. E. Stevenson, Cincinnati.—p. 893.
 Production of Collateral Circulation and Relief of Vasospasm in Peripheral Vascular Disease. L. N. Atlas, Cleveland.—p. 899.
 Classification of Tumors. L. A. Pomeroy, Cleveland.—p. 903.

Pennsylvania Medical Journal, Harrisburg

41: 969-1082 (Aug.) 1938

- Aneurysms: Statistical Study of Eighty-Four Cases from Surgical Department of Philadelphia General Hospital. E. R. Saleeby and P. A. McCarthy, Philadelphia.—p. 969.
 Some Observations Concerning Chronic Maxillary Sinusitis. H. D. Rentschler, Sayre.—p. 975.
 Treatment of Infected Abrasions of the Cornea. C. F. Kutscher, Pittsburgh.—p. 979.
 Hypothyroidism: Etiologic Factor in Eclampsia. W. B. Patterson, R. E. Nicodemus and H. F. Hunt, Danville.—p. 983.
 Plea for Conservatism in Appendectomy for Chronic Appendicitis: Observations on the Spastic, Irritable or Unstable Colon Syndrome. W. A. Swalm and L. M. Morrison, Philadelphia.—p. 988.
 Roentgenologic Diagnosis of Various Juxtadiaphragmatic Lesions, Particularly Perinephric Abscess. R. D. Bacon, Erie.—p. 992.
 Congenital Cataract. B. Chance, Philadelphia.—p. 1001.
 Value of Blood Studies in the Treatment of Lupus Erythematosus. J. J. Hecht and S. R. Perrin, Pittsburgh.—p. 1006.
 Endocrine Factors in Human Sterility: Evaluation of Diagnostic and Therapeutic Measures. C. Mazer, S. L. Israel and C. W. Charny, Philadelphia.—p. 1009.
 *Persistence of Pain Following Multiple Operations for Cure of Sinus Disease. S. R. Skillern Jr., Philadelphia.—p. 1017.
 Tumors of the Larynx, Benign and Malignant: Diagnosis, Prognosis, and Treatment. G. Tucker, Philadelphia.—p. 1023.
 Attempt to Evaluate Dyspnea by Circulation Studies in Chronic Heart and Lung Disease. E. Weiss and M. Kleinbart, Philadelphia.—p. 1026.

Pain Following Operations for Sinus Disease.—Skillern presents the variable theories on the persistence of sinus pain after operations on the sinus as expressed by sixteen leading rhinologists. A tabulation of the opinions gives the following causes in order of frequency for the persistence of pain: incomplete operation, disease elsewhere than in the sinus operated on, systemic disease causing symptoms of sinusitis, synechiae or scar tissue blocking drainage or enmeshing the nerve, direct injury to or interference with a nerve, operation on the ethmoids and turbinates for insufficient reason, individual nervous reaction to pain, neuritis of the fifth cranial nerve, atypical neuralgia of unknown origin, reaction to insult of the periosteum and bone, injury to the sympathetic plexus and diversion of normal air currents within the nose. As long as there is any evidence of sinus infection the obligations of the otolaryngologist have not been fulfilled, and the persistence of apparent sinus pain means further study in conjunction with specialists in other fields of medicine until they have found the cause and, if possible, relief has been obtained. The author believes that the persistence of pain (1) in the frontal sinus after radical operation may be due to failure to remove every

vestige of infected material, localized meningitis or osteomyelitis, abscess in the frontal lobe and/or infection in another sinus; (2) in the maxillary sinus to injury to the infra-orbital foramen, injury to the dental or infra-orbital nerve, reinfection from overlying sinuses, failure to remove all the infective material from the sinus and infection of an adjacent cell (anterior ethmoid) causing symptoms resembling those of maxillary sinusitis, and (3) in the ethmoid capsule and sphenoid sinus traumatized periosteum or bone near the foramen, direct injury to the nerves or blood vessels, proximity of the meninges (localized meningitis or osteomyelitis) and failure to open the long, narrow, fronto-ethmoid cell, the thin slitlike orbital or any anatomically misplaced ethmoid cell that may be infected. The ethmoid capsule and the sphenoid are considered as one, as synechiae may follow an operation, with the walling off of isolated areas of infection.

Public Health Reports, Washington, D. C.

53: 1337-1380 (Aug. 5) 1938

- Human Infection with *Bacillus Pseudotuberculosis* Rodentium: Case. N. H. Topping, C. E. Watts and R. D. Lillie.—p. 1340.
 Studies on Dental Caries: V. Familial Resemblance in the Caries Experience of Siblings. H. Klein and C. E. Palmer.—p. 1353.
 Unsuccessful Treatment of Malaria with Sulfonamide Compounds. G. H. Faget, M. R. Palmer and R. O. Sherwood.—p. 1364.

53: 1381-1442 (Aug. 12) 1938

- Comparison of Precipitation Reaction in Immune Serum Agar Plates with Protection of Mice by Antimeniogococcus Serum. Margaret Pittman, Sara E. Branham and Elsie M. Sockrider.—p. 1400.

Rhode Island Medical Journal, Providence

21: 113-126 (Aug.) 1938

- Surgical Aspects of Peptic Ulcer. R. Zollinger, Boston.—p. 113.
 Recent Advances in the Pathology of Diabetes Mellitus. S. Warren, Boston.—p. 117.
 Clinical Aspects of Testicular Tumors. W. C. Quinby, Boston.—p. 119.

Surgery, St. Louis

4: 161-320 (Aug.) 1938

- Delayed Operation in Treatment of Perforated Appendix. C. E. Gardner Jr., Durham, N. C.—p. 161.
 End Results Following Removal of "Inactive" Appendix. C. E. Rea and L. Kleinsasser, Minneapolis.—p. 179.
 *Tuberculous Peritonitis: Speculation on Cause of Improvement Following Surgery. M. J. Brown, Sayre, Pa.—p. 185.
 Chronic Subdural Hematoma: Diagnosis and Treatment. R. G. Coblenz, Baltimore.—p. 194.
 Subdural Hematoma, Acute and Chronic, with Some Remarks About Treatment. A. Kaplan, New York.—p. 211.
 Effect on Blood Flow of Decreasing the Lumen of a Blood Vessel. F. C. Mann, and by invitation J. F. Herrick, H. E. Essex and E. J. Baldes, Rochester, Minn.—p. 249.
 Report of 500 Blood Transfusions. E. H. Fell, Chicago.—p. 253.
 Blood Transfusion and Storage of Blood for Emergency Procedures. E. B. Tuohy, Rochester, Minn.—p. 261.

Tuberculous Peritonitis.—Since the favorable results of operation in tuberculous peritonitis are out of proportion to the amount of surgical work performed, there must be some other explanation of why these patients improve. It seems likely to Brown that in some cases equivalent improvement may be accomplished by the use of closed ether anesthesia alone. A temporary anoxemia produced by the anesthesia might be an explanation for the apparent cures. The tubercle bacilli are known to be aerobic organisms. From the known facts of culturing the tubercle bacilli, the reduced oxygen intake of the body would explain, at least partially, the improvement that follows when ether anesthesia alone is administered. The chemical study of the tubercle bacillus shows that such compounds as lipoids, fatty acids, acetone-soluble fat and wax can be isolated. Since the blood carries a large volume of ether vapor during anesthesia, it is possible that some chemical reaction may take place with one or more of these substances to cause permanent injury to the organisms or to produce an oxygen impermeable membrane about them. Such speculations on a chemical basis would tend to uphold further the proposed theory of anoxemia as an explanation of improvement in cases of tuberculous peritonitis following closed ether anesthesia alone or accompanying a surgical procedure. A study of cases of tuberculous peritonitis in which operation has been performed with spinal anesthesia would do much to settle the question of whether inhalation anesthesia is a factor in the improvement.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Journal of Ophthalmology, London

22: 449-512 (Aug.) 1938

- Rhinosporidiosis on the Eye: Case. H. Kaye.—p. 449.
Ablatio Falciformis Congenita (Retinal Fold). H. Weve.—p. 456.
Some Clinical Notes on Nature of Retinal Venous Pulse. N. Pines.—p. 470.
Lightreserve for Occupations in Sight-Saving Classes. R. A. Kaz.—p. 482.
Children with Defective Vision, in Need or Not of Sight-Saving Classes. R. A. Kaz.—p. 486.

East African Medical Journal, Nairobi

15: 95-128 (July) 1938

- Cutaneous Manifestations of Vitamin Deficiency. J. H. Sequeira.—p. 96.
Air Raid Precautions. J. R. Gregory.—p. 115.

Journal of Physiology, London

93: 75-171 (July 14) 1938

- The Carotid Sinus and Blood Regeneration. A. L. Latner.—p. 75.
Osmotic Pressure of Fetal and Maternal Serums in Sheep. E. F. McCarthy.—p. 81.
Transmission of Impulses by Ganglionic Direct Fibers. D. P. C. Lloyd.—p. 86.
Effect of Asphyxia on the Heart Rate of Rabbits at Different Ages. D. J. Bauer.—p. 90.
Segmental Distribution of Certain Visceral Afferent Neurons of the Pupillodilator Reflex in the Cat. B. A. McSwiney and S. F. Suffolk.—p. 104.
Carbonic Anhydrase Activity Inside Corpuscles. Enzyme-Substrate Accessibility Factors. V. H. Booth.—p. 117.
Action of Adrenalin, Acetylcholine and Other Substances on Nerve-Free Vessels (Human Placenta). U. S. v. Euler.—p. 129.
*Effects of Prolonged Muscular Exercise on Metabolism. J. N. Mills.—p. 144.
Action of Adrenalin in Accelerating Removal of Blood Sugar by Peripheral Tissues. H. P. Himsworth and D. B. M. Scott.—p. 159.

Exercise and Metabolism.—Mills studied the metabolism of two subjects who were not in athletic training before and after a walk of ten miles in the postabsorptive state. One subject, the author, who lived habitually on a high carbohydrate diet, showed an inconstant lowering of the respiratory quotient after the walk, but no ketonuria or depression of tolerance to dextrose, even when he restricted the carbohydrate in his diet. The other subject, who habitually consumed a lower proportion of carbohydrate, always showed a low respiratory quotient and ketosis after a walk unless he greatly increased the intake of carbohydrate in his diet. His tolerance to dextrose was considerably depressed after the walk, but if he had been living on a high carbohydrate diet this depression was absent. Curves of blood sugar have been plotted for the second subject after intravenous injection of insulin. Those after exercise did not differ from those before in the phase of falling blood sugar, showing that the depressed tolerance to dextrose was not due to a reduced sensitivity to insulin. After exercise there was, however, a delay in the return of the blood sugar to normal and determinations of respiratory exchange after injection of insulin suggested that at this time this may have been due to a higher level of carbohydrate metabolism. Insulin was found to raise the respiratory quotient much further after exercise than before.

Lancet, London

2: 235-294 (July 30) 1938

- The Approach to Gastric Surgery. W. H. Ogilvie.—p. 235.
Pneumonitis. J. Maxwell.—p. 239.
*Precision in Spinal Anesthesia. N. C. Lake.—p. 241.
*Hemolytic Streptococcus in the Etiology of Rheumatic Fever and Rheumatoid Arthritis. W. Goldie.—p. 246.
*Correction of the Sedimentation Rate for Anemia. M. Hynes and L. E. H. Whitby.—p. 249.

Precision in Spinal Anesthesia.—Lake outlines a technic for precise spinal anesthesia in the carrying out of which the patient, who may have had a preliminary injection of morphine and atropine, is given an injection of 1 grain (0.065 Gm.) of ephedrine and is then placed face downward on the operating table. Pillows are now packed under the lower part of the chest to produce a well marked dorsal curve. The back is marked with iodine to indicate the intercristal plane, the second and third lumbar interval and the seventh dorsal spinous

process. The dorsal curve is now "sighted" against a horizontal black line painted on the wall of the operating room, and the table is tilted until the marked seventh spinous process lies at the apex of the curve. The head is kept flexed well down so that no solution can reach the cervical region. By means of the same solution with a hypodermic needle a wheal is raised on the skin at the point of injection and a little of the solution is also placed along the proposed needle track. A fine-bore stainless steel needle is now introduced at this level in a direction exactly vertical to the surface in all planes. The passage of the needle should be deliberate and slow so that the penetration of the dura can be easily felt. The needle is rotated and pushed on slightly to determine that the aperture is well within the dura and it is then turned so that the lateral aperture points up the spine. A syringe is attached to the needle, care being taken that the latter suffers no displacement. The solution, 1:1,500 nupercaine in saline solution, warmed to body temperature, is injected slowly to avoid turbulence and, as far as possible, to get the nupercaine solution to travel as a "bundle" to the highest point of the theca. At least two or three minutes should be taken to introduce from 6 to 9 cc. of the solution. The quantity to be injected varies a little with the size of the patient and the nature and expected duration of the operation. When the injection is completed the needle and syringe are held steady for a further thirty seconds and then withdrawn. The patient now remains in the same posture without movement for ten minutes and is then turned on his back, the pillows being removed and the table tilted into the head-down position. The operation may be immediately started. The author has now used this technic for nearly three years in many hundreds of cases and has obtained uniformly good results. It requires no complicated apparatus beyond the ordinary tilting operating table. Severe headaches are rare and there have been no other neurologic sequelae.

Hemolytic Streptococcus and Rheumatism.—Goldie states that there is clinical, immunologic and pathologic evidence of an etiologic relationship between rheumatic fever and rheumatoid arthritis. Immunologic data are presented to show that infection with the hemolytic streptococcus is more prevalent in these two diseases than in normal persons. Myocardial changes showing some resemblance to those characteristic of rheumatic fever have been produced in animals sensitized to bacterial protein, and this lends support to the theory that rheumatic fever and rheumatoid arthritis result from sensitization to the hemolytic streptococcus.

Sedimentation Rate and Anemia.—Hynes and Whitby constructed "sedimentation curves" according to the method of Wintrobe and Landsberg (1935). From observations of thirty-eight normal students a normal curve was constructed and the limits of the normal sedimentation rate were confirmed. Curves were made from forty-six cases with abnormal sedimentation rates. Curves were also made from eleven anemic patients whose blood, when reconstructed and rendered nonanemic by the addition of corpuscles, had normal sedimentation rates. These curves, whatever the degree of anemia, were precisely of the type obtained from normal students with similar sedimentation rates. In the same way the degree of anemia was found not to influence the shape of the curves for cases with abnormal sedimentation rates of the same order. These facts confirm the principle of correcting the sedimentation rate for anemia in terms of the hematocrit reading according to the method of Wintrobe and Landsberg.

Medical Journal of Australia, Sydney

2: 71-108 (July 16) 1938

- Early Diagnosis of Cancer of Cervix. H. H. Schlink and C. L. Chapman.—p. 71.
Treatment of Cancer of Cervix Uteri. H. H. Schlink and C. L. Chapman.—p. 74.
Casualty Surgery. A. Aspinall.—p. 81.
Manipulative Surgery. W. K. Hughes.—p. 83.
The Contact Lens. J. D. Maude.—p. 85.
X-Ray Therapy in Sinusitis. H. Mitchell.—p. 86.
Blood Uric Acid Estimation in Eclampsia. T. Rose.—p. 87.
Fractures of the Spine, with Special Reference to Laminectomy. N. Little.—p. 89.
Analysis of Autopsy Findings in 200 Cases of Pulmonary Tuberculosis. A. H. Penington.—p. 90.

Journal Belge de Neurol. et de Psychiat., Brussels

38: 495-558 (July) 1938. Partial Index

- Nontraumatic Intracerebral Hematoma: Operation and Cure. L. Laruelle and L. Massion-Verniory.—p. 495.
 Pathogenesis of Vestibular Disturbances in Lesions of Spinal Cord. J. Helmsmoortel Jr.—p. 504.
 *Prospects of Survival and Cure in Dementia Paralytica: Eighty Calamities Ten Years After Malarial Therapy. P. Vervaeck.—p. 508.
 Vertebral Anomalies and Radicular Disturbances. M. Leroy.—p. 520.
 Value of Metrazol Test in Diagnosis of Epilepsy. G. Muyle.—p. 525.

Survival and Cure in Dementia Paralytica.—Vervaeck points out that the majority of about 2,000 publications that have appeared since the beginning of the era of malaria therapy of dementia paralytica is concerned with the clinical and social results of this treatment. Reviewing the figures given by different investigators about the percentages of remissions obtained with this treatment, the author found that they differ widely. He investigated the condition of patients with dementia paralytica ten years after they had been treated at a psychiatric clinic in Brussels. Investigations were made on the men who had been treated during the years 1926 and 1927. Dementia paralytica being less frequent in women, the follow-up studies were extended to the female patients who received treatment during the four years from 1925 to 1928 inclusive. Of fifty male patients, forty-one had been subjected to malaria therapy; and of fifty-three women, forty-two had been so treated. Of the forty-one male patients who had been treated with malaria, seven were still outside an asylum ten years after, but one of these died two months later, aged 53; four others had died outside an asylum, one of them after a second sojourn there; one lives in an asylum, again demented after having been at liberty for two years; seven died in an asylum where they had been returned; seven live in an asylum which they were never able to leave; thirteen died in the asylum, never having left it; two disappeared, and one of these was probably cured. Evaluating these results, the author concludes that in 64 per cent of the men with dementia paralytica who had been subjected to malaria therapy the results were unfavorable. After citing the later fate of the forty-two women with dementia paralytica who had received malaria therapy, the author shows that among these the frankly unfavorable results likewise amounted to 64 per cent.

Presse Médicale, Paris

46: 1209-1224 (Aug. 6) 1938

- Effect of Fluid Diet and of Blood Loss on Development of Typhoid. L. Ambard, P. Barthelme and P. Mandel.—p. 1209.
 *Acetarson Therapy of Dementia Paralytica. L. Marchand.—p. 1211.

Acetarson Therapy of Dementia Paralytica.—Marchand's report is based on the results obtained with acetarson in the treatment of 111 patients with dementia paralytica. None of the patients treated were, or had been, subjected to malaria therapy. Three times a week the patients were given a subcutaneous injection of 1 Gm. of sodium acetarson dissolved in 10 cc. of distilled water. The total for a series of treatments was 45 Gm. The series were separated by intervals of three or four weeks. In the first two injections only half of the dose, that is 0.5 Gm., was given, in order to test the sensitivity of the patient. During the first few weeks of treatment the patients were kept in bed. The number of series of treatments required varies in different patients. Some of the patients are able to leave the hospital after the first series. In some of the patients, in whom the dementia paralytica advanced rapidly, the author intercalated between the acetarson injections an injection of quinine bismuth iodide until a gingival border appeared. Tests for syphilis were made on the blood and on the cerebrospinal fluid, before as well as after the treatment. The temperature was measured every day and the weight was determined before the treatment and then every month. An examination of the fundus oculi was made before the treatment and every two weeks thereafter. The author lists the results of the treatment in a tabular report. He says that he obtained "social recuperation" in seventy-one (64 per cent) of the 111 patients and improvement in ten patients (9 per cent); fifteen patients (13.5 per cent) died. The author speaks of "social recuperation" in those patients in whom the mental defects have disappeared so that they are able to resume their former occu-

pations but who are not cured organically. The social recuperation was obtained in twenty-six patients after one series of treatments, in twenty-six after two series, in eleven after three series, in six after four series and in two after five series. Following a discussion of the behavior of the reactions in the blood and in the cerebrospinal fluid in the patients in whom social recuperation was obtained, the author discusses the relapses. He says that nine of these patients had to be hospitalized again, because of the recurrence of mental disturbances. The relapses are due to a premature arrest of the treatment, to an insufficiency of the doses or to excessive length of the intervals between the series of injections. The patients with dementia paralytica who have been treated with acetarson should be kept under clinical and serologic control for several years after the treatment. The complications that may appear in the treatment with acetarson are slight in comparison to the severity of the disease. Discussing the contraindications to treatment with acetarson, the author says that the treatment should be avoided in senile subjects who present organic difficulties. However, tabetic symptoms and alcoholism without hepatic insufficiency do not constitute contraindications to treatment with acetarson.

Sang, Paris

12: 677-780 (No. 7) 1938

- New Applications of Karyoklastic Poisons to Experimental Pathology, Endocrinology and Cancerology. A.-P. Dustin.—p. 677.
 New Method of Examination of Coagulability of Blood (Coaguloretravismetry). L. Blacher.—p. 698.
 *Hepatic Opothrapy and Cholesteremia: Experimental Study. P. Van de Calseyde.—p. 712.

Hepatic Opothrapy and Cholesteremia.—Van de Calseyde reports experimental studies on the effect of liver therapy on cholesteremia. Studies were made on human subjects as well as on animals. It was found that it is not possible to determine the antianemic power of liver preparations on the basis of the variations in the cholesteremia which they engender in normal human subjects and animals. There is no parallelism between the variations in the cholesterol content and the antianemic power of the extracts. Nevertheless the author thinks that his observations on the hypercholesteremia produced by the ingestion of whole fresh liver or of certain liver extracts used for the treatment of pernicious anemia is of considerable biologic interest. His investigations proved that the increase in cholesterol is not due to the factor that exerts the therapeutic action in pernicious anemia, to the cholesterol content of the liver or to the vitamin A content of the liver. The appearance of the increase in cholesterol after ingestion of hydrosoluble extracts prepared according to the methods of Cohn and Gänsslen seemingly indicates that the agent inducing hypercholesteremia is neither a lipid nor a protein. Further investigations will be necessary to determine the chemical nature of the hypercholesterolizing factor of the liver. Other questions that await answers are: Is this substance present in tissues other than those of the liver? Is it related to the vitamins or hormones? By what mechanism does it increase the cholesterol content?

Annali Italiani di Chirurgia, Bologna

17: 525-666 (June-July) 1938. Partial Index

- *Metabolism of Nitrogen and Chlorides After Injection of Normal Blood Serum of Horse. G. Conti.—p. 525.
 Physical and Chemical Values of Blood in Experimental Burns. G. Prussia.—p. 543.
 Influence of Intermittent Interruption of Arterial and Venous Circulation on Development of Renal Pyogenic Infection. P. Bassi.—p. 557.
 Hemoperitoneum from Rupture of Nonpregnant Corpus Luteum: Case. S. Caminiti.—p. 639.

Metabolism After Injections of Horse Serum.—Conti observed the behavior of nitrogen and chlorides in the blood and of urea, uric acid and the chlorides in the urine of twelve normal persons who were given intramuscular injections of from 20 to 50 cc. of normal horse serum. The injections were administered at intervals of twelve hours until 140 cc. had been given. In all cases the injection was followed by increased azotemia, increased elimination of urea, uric acid and the chlorides in the urine and lowering of the chlorides in the blood. According to the author the results show that the proteins in the serum are disintegrated and eliminated shortly after the injection in a

similar manner to that which takes place in plasma proteins after transfusion. The results confirm the author's opinion that the plasma has a mechanical action on the blood, that the plasma proteins are disintegrated and eliminated shortly after transfusion and that disintegration of the erythrocytes takes place several days after transfusion with consequent liberation of erythrocytic proteins which are used by the blood. Assimilation of erythrocytic proteins reestablishes the equilibrium of the blood.

Bollettino, Milan

12: 85-148 (April-June) 1938. Partial Index

- Early Diagnosis of Extrapulmonary Tuberculosis. A. Isella.—p. 93.
Isolated Fracture of Transverse Apophysis of Lumbar Vertebra: Case. M. Manfredi.—p. 105.
*Galvanocautery Puncture in Suppurative, Acute Lymphadenitis of Neck in Infants. G. Cigada.—p. 113.

Galvanocautery Puncture in Lymphadenitis in Infants.—Cigada reports satisfactory results from puncture by means of the galvanocautery in twenty-seven cases of either acute abscess or acute suppurated lymphadenitis of the neck. Both the therapeutic and the cosmetic results are satisfactory. The tiny scars left by the puncture are almost invisible and they disappear in a few months. Puncture by the galvanocautery has no contraindications. It is done without anesthesia. The perforations remain open all through the process of elimination of pus. It gives more rapid results than many of the other treatments commonly resorted to in these conditions. As a rule it suffices for complete elimination of the pus. The best results are obtained when the pus is in a circumscribed cavity or when the different cavities of an abscess are punctured and also when the pus is already near the superficial layers of the tissues. It is advisable to use galvanocautery needles of medium size in order to make well opened outlets for rapid and sufficient elimination of pus. Local hot applications and complementary treatments (vaccines) are indicated. The total number of perforations is from three to five. Only in rare cases is reopening of the perforations or a surgical incision necessary. The treatment is well tolerated by infants and children.

Polislinico, Rome

45: 1553-1592 (Aug. 22) 1938. Practical Section

- *Action of Thymus on Blood and Spleen. S. De Candia and F. Floriani.—p. 1553.
Liver Lipolytic Enzymes in Therapy of Nutritional Diseases in Children. N. Amagliani.—p. 1556.
Epinephrine Treatment of Malaria. V. Romeo.—p. 1562.

Action of Thymus on Blood Formation.—De Candia and Floriani observed the behavior of the blood and of the spleen in twenty normal persons with normal sized spleen after an intramuscular injection of 2 cc. of thymus extract which contained 1 Gm. of fresh gland for each cubic centimeter of the extract. The observations were made during fasting. Determinations of the changes of the blood and of the spleen were made half an hour and one hour after the injection. The erythrocytes and the leukocytes, but principally the former, increased during the first hour. The leukocytic formula gave different results in various persons of the group. There was an increase of the monocytes and parallel diminution of the neutrophilic polynucleated leukocytes in some cases, moderate increase of either the lymphocytes or the neutrophilic polynucleated leukocytes in other cases and the leukocytic formula did not change at all in still other cases. In all cases the size of the spleen diminished during the first hour following the injection (3 cm. in the longitudinal diameter and 2 cm. in the transverse diameter) and the diminution lasted for more than an hour. In two groups of patients (the number of which is not specified by the author) suffering from either fibrous forms of splenomegaly (Laënnec liver cirrhosis, Banti's disease and bantiform syndromes) or malarial splenomegaly, they found that the size of the spleen did not change or had a slight change in fibrous forms of splenomegaly, whereas the injection induced a more or less energetic contraction of the spleen, which lasted for more than an hour in the group of patients who were suffering from malarial splenomegaly. The authors believe that the intramuscular injection of thymus extract can be used for the differential diagnosis between fibrous and malarial forms of splenomegaly. It can be used also instead of epinephrine in the treatment of malarial splenomegaly by means of repeated induced contraction of the spleen.

Archiv für Gynäkologie, Berlin

167: 253-396 (July 20) 1938. Partial Index

- Pregnancy Intoxication Simulating Tabes Dorsalis. H. Offergeld.—p. 275.
Method of Testing Echolic Substances on Vagina of Rabbits. H. Runge, W. Beck and E. Hunt.—p. 284.
Tubal Pregnancy and Reaction According to Aschheim-Zondek. H. Klinkenberg.—p. 300.
Significance of Uterus and Adrenals for Luteinization. W. Wobker.—p. 339.
Interstitial Pregnancy. T. K. Andrianakos.—p. 343.
*Proliferation of Uterine Mucosa in Case of Intra-Uterine Administration of Estrogen. P. Grumbrecht and A. Loeser.—p. 373.
Significance of Vegetative Nervous System for Incretory Function of Anterior Lobe of Hypophysis. L. Herold and G. Effkemann.—p. 389.

Intra-Uterine Administration of Estrogen.—Grumbrecht and Loeser say that experimental studies on the pathology and therapy of ovarian insufficiency revealed that the requirements for the action of estrogen on the various organs differ considerably. For instance, whereas the castration atrophy of the sex organs can be counteracted by the parenteral administration of estrogen, the changes which castration produces in the thyroid can be counteracted only if the substance is administered by way of the uterus. If it is administered by any other than the uterine route, it exerts no influence on the thyroid. The authors studied the reaction of the uterus to the local application of various estrogenic substances. They made experiments on infantile rats and guinea pigs and on mature rats. They found that the intra-uterine application of different estrogenic substances produces proliferation of the uterine mucosa with smaller doses and in a much shorter time than is the case in subcutaneous administration. The observations in the course of the animal experiments suggested to the authors the possibility of the clinicotherapeutic utilization of the intra-uterine administration of estrogen. For use in human subjects they employed suppositories which were from 4 to 5 cm. in length and a few millimeters in thickness. Each suppository contained 500 international units of estrogenic substance in a base of theobroma oil. The suppositories were sterile and were stored on ice. The authors say that their introduction into the internal uterine os was not difficult. In order to prevent the slipping back, a strip of gauze was introduced into the cervical canal for three or four hours. With this mode of application, undesirable complications such as increase in temperature, pains or local irritations were avoided. The case histories reported by the authors indicate that the intra-uterine administration of estrogenic substance is effective in cases of hypomenorrhea and secondary amenorrhea and in uterine hypoplasia with ovarian insufficiency and oligomenorrhea.

Deutsche Zeitschrift für Nervenheilkunde, Berlin

147: 1-136 (July 18) 1938

- *Symptomatology and Pathogenesis of Lumbosacral Neuritis. H. Pette and P. E. Becker.—p. 1.
Myoclonic Syndrome in Amyotrophic Lateral Sclerosis. G. Doring.—p. 26.
Electromyographic Investigations on Thomsen's Myotonia and Dystrophia Myotonica. W. Eichler and I. von Hattingsberg.—p. 36.
Head's Zones. H. Plügge.—p. 78.
Observations on Reduction of Muscular Activity in Myasthenia Gravis. W. Birkmayer.—p. 118.

Lumbosacral Neuritis.—Pette and Becker show that lumbosacral neuritis is a definite disease entity. On the basis of nine selected cases, they demonstrate the different forms the disease may take as regards the symptomatology and the course. The subjective and objective symptoms indicate that the morphologic changes, although as yet they have not been verified by anatomic studies, are chiefly in the region of the sympathetic centers and tracts. The clinical aspects, together with the somewhat characteristic changes in the cerebrospinal fluid, suggest that the disorder is an inflammatory process of spinal ganglions in the region of the lumbosacral plexus. Accordingly the authors designate it as a neuritis of the lumbosacral plexus. The disorder is closely connected with herpes zoster, they say, and consequently it can be classified with the group of virus diseases of the nervous system. The as yet hypothetical causal agent is characterized by neurotropic properties. As in other virus diseases of the nervous system (poliomyelitis, rabies), the term neurotropism is applicable in its restricted sense in lumbosacral neuritis. From the fact that a predisposition to so-called

rheumatic disorders and to excessive sympathetic reactions is frequently observed not only in the patients themselves but also in members of their families, the authors conclude that constitutional factors play a part in the pathogenesis of lumbosacral neuritis.

Münchener medizinische Wochenschrift, Munich

85: 1137-1176 (July 29) 1938. Partial Index

Question of Existence in Germany of an Encephalitis of the Character of Encephalitis Japonica. H. Pettc.—p. 1137.

Pathogenesis of Scarlet Fever in Persons Who Have Not Been in Contact with Scarlet Fever Patients. W. Schultz.—p. 1140.

*Types of Diphtheria Bacilli and Clinical Course of Diphtheria in Children. S. Werner.—p. 1141.

Observations on Kala-Azar in Children in Province of Argolis in Greece. S. D. Kirimlidis.—p. 1143.

Deficiency of Vitamin B₁ or Rheumatism. A. Nemecek.—p. 1147.

*Angina Pectoris with Fatal Outcome Elicited by Inhalation of Hydrogen Sulfide Gas: Case. A. Hellfors.—p. 1149.

Neurology and Neurosurgery of Angina Pectoris. H. Jessen.—p. 1149.

Types of Diphtheria Bacilli and Course of Diphtheria.

—Werner says that among 134 cases of diphtheria in which the type of bacillus was determined there were eighty-four cases with the type gravis, forty-two cases with the type intermedius and eight cases with the type mitis. A relationship between the course of the disease and the type of the diphtheria bacillus could not be detected. There was no evidence that one type of bacillus would cause a severe form of diphtheria and another type a mild form. A change in the type of bacilli was observed in 9.7 per cent of the children; in all others the same type of bacillus was detected throughout the entire course of the disease. It was not possible to furnish definite proof of a real change in type. Since the available space did not permit a segregation of the patients according to the type of bacillus, there was always a possibility of superinfection with another type of bacillus. The persistence of positive smear tests was considerably longer in the patients in whom the gravis type of bacillus was present than in the patients with the intermedius type.

Inhalation of Hydrogen Sulfide Gas.—Hellfors reports the history of a man aged 63 who had angina pectoris after he had inhaled hydrogen sulfide gases while he was conducting experiments. In response to treatment the attacks of angina pectoris subsided somewhat but they recurred after renewed exertion. Then the patient contracted influenza, in the course of which the angina pectoris was aggravated. He died in a severe attack of angina pectoris. On the basis of this case history, the author suggests that the angina pectoris-like pains which are observed in persons with similar intoxications are due to temporary circulatory disturbances in the coronary vessels. He admits that two brothers of this patient likewise had angina pectoris, but he nevertheless thinks that the hydrogen sulfide intoxication was the eliciting factor of the angina pectoris in the reported case, because fourteen months previously the patient had a slightly increased blood pressure but no signs of coronary disease.

Nederlandsch Tijdschrift v. Geneeskunde, Amsterdam

82: 3647-3718 (July 23) 1938. Partial Index

*Blood Group and Diameter of Erythrocytes. Tjiook Kiem Bok.—p. 3657.

Echinococcus in Central Nervous System. M. Weersma.—p. 3662.

Anterior and Posterior Rachischisis. A. J. P. Van Den Broek and S. Van Dam.—p. 3666.

Blood Group and Diameter of Erythrocytes.—Tjiook Kiem Bok was induced to investigate a possible relationship between the blood group and the mean diameter of erythrocytes by a report of Pijper, who in studies on forty-eight cases was believed to have found evidence of such a relationship. Tjiook Kiem Bok made his tests on 500 healthy persons (students, nurses and laboratory staff). He determined the four classic blood groups and the mean diameter of the erythrocytes, respectively, by the method of Moss, Lee and Vincent and the diffraction method, using Pijper's blood cell tester. From this investigation the following conclusions could be drawn: 1. A correlation between blood group and red cell diameter, as Pijper assumed, could not be demonstrated. 2. The mean diameter of the erythrocytes of these persons is 7.3 microns, with a normal range of from 6.8 to 7.9 microns. 3. Sex has no influence on the mean diameter.

Nordisk Medicinsk Tidskrift, Stockholm

16: 1125-1164 (July 16) 1938

*Boeck's Iritis. G. Østerberg.—p. 1125.

Electric Shock: Significance of Different Technical Factors and of Individual Resistance in Accidents Due to Electric Shock. H. Ihde.—p. 1132.

Simplified Method for Diagnosis of Pregnancy According to Kapeller-Adler. N. Nielsen.—p. 1144.

Boeck's Iritis.—Østerberg describes the case of a girl, aged 14, in whom a torpid, indolent monocular nodulous iritis developed and in the course of a year reduced the vision to 2/50 and threatened perforation of the eye. Enucleation was contemplated. There were no pulmonary symptoms but the roentgenogram of the lungs resembled a miliary tuberculosis and operation was deferred. In the course of nine months spontaneous recovery of the eye occurred, with restoration of vision and of the exterior of the eye almost to normal, and spontaneous regression of the pulmonary changes. Microscopic examination of tissue from an apparently healthy tonsil demonstrated sarcoid of Boeck. The author asserts that there is a distinct Boeck's iritis which is not identical with iritis tuberculosa; it is less painful, less destructive and more proliferative than iritis tuberculosa. The differential diagnosis must be based on the patient's general condition and the tuberculin, roentgen and microscopic examinations. Iritis is a relatively rare symptom in Boeck's disease, occurring in from about 5 to 10 per cent. Twenty-seven cases of Boeck's disease with iritis are tabulated from the literature.

Ugeskrift for Læger, Copenhagen

100: 749-776 (July 7) 1938

Hand-Schüller-Christian Syndrome: Case. E. Warburg.—p. 749.

Monocytic Leukemia (Reticulo-Endotheliosis): Three Cases. P. Plum and S. Thomsen.—p. 755.

*Solitary Nonparasitic Hepatic Cysts. I. Baumgarten.—p. 762.

*Heerfordt's Syndrome (Uveoparotid Fever), Manifestation of Boeck's Sarcoid. M. Jersild.—p. 765.

Solitary Nonparasitic Hepatic Cysts.—Baumgarten says that about 100 cases of solitary nonparasitic hepatic cysts have been reported in the literature since 1864. The majority of the cysts are caused by retention in the bile ducts, due to congenital malformation or to local obstruction of small intra-hepatic bile ducts. Most of them give no symptoms. If symptoms do occur, they are usually due to pressure on neighboring organs. Exact diagnosis is rarely made before operation or necropsy. The only effective therapy is surgical intervention, and the ideal operation is extirpation. The highest operative mortality occurs in cases in which puncture is done, the lowest in radical operations. In the case reported, in a woman aged 26, extirpation of the cyst was followed by recovery.

Heerfordt's Syndrome.—In Jersild's two cases of Heerfordt's syndrome the roentgenologic changes in the lungs led to the diagnosis of sarcoid of Boeck. In spite of the extensive processes the patients felt remarkably well and the Mantoux reaction, as frequently described in cases of sarcoid of Boeck and Heerfordt's syndrome, was positive only on larger doses of tuberculin. In one case with exanthem, biopsy supported the diagnosis. The author suggests that, since the etiology of sarcoid of Boeck is not clear, the relation of the disease to uveoparotid fever, which generally appears as an infectious disease with acute onset, may open new perspectives. Heerfordt's syndrome, he says, is surely the initial stage in a long-continued chronic infectious disease.

100: 777-806 (July 14) 1938

*Investigations on Etiology of Epidemic Hepatitis. T. T. Andersen.—p. 777.

Etiology of Epidemic Hepatitis.—Andersen asserts that jaundice in swine, contrary to the common conception, is a parenchymatous liver disorder corresponding to hepatitis in man and is transmissible to other swine and other animals, which demonstrates the infectious nature of the disorder. His investigations also show that hepatitis in swine probably originates from a similar latent infection in rats. Since there is hepatitis in swine and since, according to statistical studies, an alimentary infection is probable in man, he is inclined to believe that hepatitis in swine is one of the causes of hepatitis in man and is in Denmark presumably the most important cause.

THE STUDENT SECTION

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Obstetric Education

EDWIN F. DAILY, M.D.

CHICAGO

The practice of medicine in America has been the subject of discussion, praise and criticism during the past few years perhaps to a greater extent than during any previous comparable period of time. At no time in our history have American physicians been so aware of the interest of the people in the quality and quantity of medical services available.

The interest always manifested in the illness and death of mothers and infants has resulted in numerous studies of the underlying factors causing the maternal and infant mortality in different parts of the United States. The results of these studies made by medical specialists in their respective fields have been constantly brought to the attention of both the medical profession and the public.

The White House Conference in 1930 studied all phases of the problem and published many volumes which are valuable sources of factual information. Following the exhaustive study of maternal mortality in fifteen states made by the Children's Bureau, maternal-mortality surveys were made in many states and in many of the larger cities in the United States. The results and conclusions of all these studies are remarkably alike. Analyses have been made of all factors concerned in maternal mortality, and the responsibility assigned to the physician has not been small. The fact that lack of judgment or negligence on the part of the physician is responsible for a portion of the maternal deaths in the United States has caused not a little concern but has resulted in few constructive programs for improving the situation. In the last generation there has been considerable improvement in the care received by maternity patients in this country, but this improvement has not kept pace with that of most of the other medical specialties.

The art of obstetrics has been considered strictly as a part of medical practice in the United States and without doubt it will con-

tinue to become increasingly so in the future. No one who is familiar with the high professional standards of the medical profession in the United States doubts that the average physician practicing obstetrics renders service to the best of his ability and knowledge. Since the quality of obstetric care received by a patient depends primarily on the amount and type of education and experience her physician has had in this specialty, we are concerned primarily with a consideration of these subjects. There can be no doubt that if every physician practicing obstetrics had a thorough basic knowledge of antepartum care and of the conduct of labor there would be fewer tragedies of childbirth.

The Council on Medical Education and Hospitals of the American Medical Association reported in 1937 that "the teaching of obstetrics is at a lower level than that of the other major clinical departments. Comparatively few schools offer to their students an adequate practical experience under competent supervision. This may result from a variety of causes, one of which is, undoubtedly, the failure of administrative authorities to provide access to a sufficient amount of clinical material. Another may be the feeling on the part of teachers that the practice of obstetrics should be reserved for specialists and that therefore the ordinary undergraduate does not need much training along this line."

Eight years ago the White House Conference Committee on Obstetric Teaching and Education stated that:

The better the clinical training of students in the art of obstetrics, the better obstetrics they will practice, and this in turn will be reflected in improved results. . . . The need is not for less theory but more clinical instruction. . . . In so far as obstetrics is concerned, the majority of students at the time of graduation are not qualified to assume the responsibilities of caring for maternity cases. . . . They may have had in most instances sufficient theoretical training but they lack actual experience. It is obvious, then, that obstetric educational facilities in this country have been entirely inadequate in so far as the teaching of actual delivery care is concerned. There have been and still are too few well organized women's

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clinics in connection with medical schools to give the necessary training and experience to medical students, to say nothing of the dearth of facilities for developing specialists in this field.

Few medical schools today have sufficient clinical obstetric material available for the instruction and training of their students in antepartum, delivery and postpartum care. The importance of such instruction and training is illustrated by the fact that in a Midwestern state, according to a recent survey, more than 50 per cent of the physicians include obstetrics in their practice.

Dr. W. C. Danforth, chairman of the Illinois Committee on Maternal Welfare, wrote in 1936:

The ideal remedy for the high maternal mortality in this country would be to provide obstetric attendance and well equipped hospitals in which women in labor may be cared for. This ideal state of affairs will not arrive for a long time but gestation and labor will continue.

Some attempt must be made to improve the present conditions while we wait for the changes which time will no doubt bring. For many years, in any event, most of the women in the majority of our states will continue to be cared for by general practitioners. It is not fair to demand of the man in family practice the same familiarity with and skill in the handling of all the obstetric problems which are sometimes presented. He must also meet medical problems in many other fields, and the incessant demands upon his time, if he is a successful practitioner, make a minute knowledge of any special field impossible. In many communities, in our own state as in others, the general practitioner may be compelled to meet situations which would tax the skill of the specialist in his fully equipped hospital, assisted by a trained personnel. Without special knowledge, lacking trained assistance and the material resources of a hospital equipped to deal with obstetric emergencies, he cannot be too greatly criticized if, in some cases, his results are not ideal. He must, however, have sound fundamental knowledge of obstetrics and realize not only what it is wise to do but also what it is unsafe to attempt.

Before considering what changes might be desirable in obstetric education, let us review a few facts concerning the education now provided.

A recent Children's Bureau questionnaire answered by 2,538 graduates of sixty-one medical schools in 1936 revealed that with regard to the study of obstetrics:

Lectures were begun by 44 per cent in the second year.

Lectures were begun by 55 per cent in the third year.

Clinical training was begun by 4 per cent in the second year.

Clinical training was begun by 70 per cent in the third year.

Clinical training was begun by 25 per cent in the fourth year.

Practically 100 per cent reported that their clinical training included examination and care of women during pregnancy, labor and the postpartum period. This survey shows that didactic and clinical obstetric teaching begins during the second or third year in most medical schools; it does not, of course, reveal the amount

of instruction given or the knowledge of the instructors of the principles of obstetrics as applied to actual practice. As Dr. Weiskotten pointed out in his survey of medical schools: "It would appear that in many instances far too little attention has been given to the selection of the faculty. It is safe to assume that a teacher should have some special preparation and that an individual who has had no such training or experience in a subject is not competent to teach it." The failure of some schools to teach students how to practice obstetrics in the best interests of their patients under the conditions they must work under in homes and in small hospitals is responsible in no small part for their difficulties in later practice.

STUDENTS' CLINICAL EXPERIENCE

Concerning their clinical experience while in medical school, the 2,538 recent graduates reported the facts presented in table 1.

The "Essentials of an Acceptable Medical School," approved by the House of Delegates of the American Medical Association, states that every medical student should have actual charge of fifteen maternity patients under the supervision of a clinical instructor, yet 19 per cent of these students delivered no patients in hospitals and 27 per cent had no home deliveries as part of their training. Fifty-nine per cent of the students had a total of twenty or fewer deliveries in hospitals and homes. Twenty-three per cent of the students reported delivering ten or fewer patients in hospitals and homes.

The number of patients a student delivers is in itself no indication of the clinical training received, for without competent instruction and supervision the experience is of little value. However, with so few actual deliveries by students it is obvious that the amount of experience and instruction must be extremely limited for a large proportion of the students.

According to the "Essentials of a Hospital Approved for Training Interns," prepared by the Council on Medical Education and Hospitals of the American Medical Association in 1935, an intern should deliver at least ten patients while in the service. Concerning their obstetric experience during internship, the recent graduates referred to reported the facts given in table 2.

Twenty-two per cent reported delivering ten or fewer patients in home and hospital during their internship.

Thirty-two per cent reported delivering twenty or fewer patients in home and hospital during their internship.

Of the interns who attended hospital deliveries, 22 per cent reported that their deliveries were not supervised by an obstetrician.

Seventy-two per cent of these graduates plan to include obstetrics in their practice and 15 per cent plan to specialize in obstetrics. Eighteen

per cent of them did not believe that their obstetric training in medical school and during internship qualified them to include obstetrics in their practice. Sixty-three per cent of them wished to receive more obstetric training, and 23 per cent reported that they were unable to do so because of too few hospital appointments in this field.

There are only eighty-eight approved hospitals in the United States admitting more than a thousand patients annually which offer residencies in obstetrics or obstetrics and gynecol-

TABLE 1.—*Deliveries by Medical Students*

	0	1-10	11-20	More Than 20
Number of deliveries.....	0	1-10	11-20	More Than 20
Percentage of students delivering this number in hospitals.....	19	49	17	15
Percentage of students delivering this number in homes.....	27	43	22	8

ogy. Only forty-three of this number offer both resident and assistant resident positions. In these hospitals there are only about 150 resident or assistant resident appointments in obstetrics and obstetrics and gynecology made each year.

One inescapable conclusion of this questionnaire study of obstetric education is that the average physician entering practice today does not have sufficient clinical training in obstetrics to recognize and treat competently the many complications that may arise during pregnancy and labor. The importance of this conclusion is emphasized by the limited number of specialists in obstetrics, most of whom are concentrated in a few large cities.

GRADUATE STUDY

Attempts to provide postgraduate lecture courses in obstetrics for local practicing physicians have accomplished little more than to make the individual physician realize more than ever his inability to provide competent obstetric care. There has been a great demand from these physicians for opportunities to return to clinical teaching centers for further training. Most of them have been disappointed, for there are few places where they may go for such training. Opportunities for practicing physicians to return to the larger teaching hospitals have been provided to a certain extent in several states and an increase in the number of these may be expected in the near future.

The problem confronting certain medical schools is the difficulty in making sufficient clinical obstetric material available for all the students. This lack of teaching material cannot be remedied easily, if at all, in many medical schools.

The establishment of a few maternity centers primarily for teaching purposes in selected areas, especially in the South, would provide opportunities for additional clinical training for

many students and practicing physicians. These maternity centers should provide care for the medically indigent patient and afford opportunities for research, and should be supported by public funds. The greatest difficulty in establishing such centers would be encountered in staffing them with instructors who are willing and competent to teach sound, conservative, routine obstetrics rather than to demonstrate their surgical skill or unusual cases of great interest to them but of little practical teaching value.

In order to provide competent medical care for a larger proportion of maternity patients, either there must be greater opportunity for obstetric training before graduation and during internship, or the practice of obstetrics must gradually be limited to those men who have had opportunities for special training in obstetrics subsequent to their ordinary internship. Every effort should be made to increase the number of resident appointments in hospitals with maternity services and to secure the services of the best obstetricians in the community to teach and supervise the work of the interns and residents.

Whatever progress in obstetric education is to occur in the near future will depend to a great extent on the study and careful consideration by every one concerned in the teaching of obstetrics of (1) the instruction and training now given medical students and graduates and (2) the results of the services these physicians render their patients when in practice.

The importance of adequate instruction for undergraduate and graduate students has been recognized and stressed by teachers of obstet-

TABLE 2.—*Deliveries by Interns*

	0	1-10	11-20	More Than 20
Number of patients delivered.....	0	1-10	11-20	More Than 20
Percentage delivering this number in homes during internship	82	13	2	3
Percentage delivering this number in hospitals during internship.....	15	9	10	66

rics for many years. Unfortunately the tremendous social importance of such instruction is not recognized by teachers in other medical fields and by the administrators of medical schools who listen to but do not act effectively in carrying out programs of obstetric education advocated by teachers of obstetrics.

If obstetrics is to maintain its position as a recognized medical specialty in the United States, our physicians must receive sufficient undergraduate and graduate training to enable them to guide their patients safely through pregnancy, to conduct deliveries with the skill and judgment required, and to recognize the value of expert consultation when complications arise.

Comments and Reviews

THE ART AND TECHNIC OF STUDY

Thousands of students are at present returning to medical schools throughout the United States to continue their studies or to engage in the study of medicine for the first time. Each one of the various medical curriculums will require of the students great concentration of effort and continuity of attention. In this long process the students naturally will acquire habits of study, and it seems desirable for them to be guided by certain general principles which may increase their efficiency and make more effective the hours of study. Such is the intention of the following opinions of some writers who have given special attention to the technic of study.

Walker¹ points out that medical students are far too ready to slump into a condition of subnormal physical health. A reaction tends to set in early against the athletic activity of the public schools when undergraduate life is reached, but sound physical health must be maintained. The rich opportunities given by university life for the preservation of physical fitness should be exploited fully. A certain proportion of each week and each year should be set aside exclusively for recreation. Of equal importance is the development of mental stamina, which term includes not only the acquisition and maintenance of will and judgment, remote alike from rashness and pusillanimity, nor merely the ability to sacrifice the present to the future, but also the cultivation of the gentler arts of the world. Medicine may be a jealous mistress, but he who gives her his all will never experience the contentment and philosophical security which a broad general culture imparts. During the student years, time must be found for the study of a science for its own sake—any subject which appeals to the individual—or for the cultivation of literature or an art. The necessity for travel in the student years must be mentioned. During these tours, either at home or abroad, there can be no harm in visiting the hospitals and schools; but any attempt at promiscuous study, Walker believes, should be suppressed.

In the study of medicine much knowledge has to be acquired in a relatively short time. While it is necessary to know, for example, that the islets of Langerhans are not in Polynesia, loading up with necessary facts is by no means the most important part of the curriculum. Much more important is the acquisition of technical

skill, dexterity, practical experience and clinical acumen. Of greater importance still is the keeping of a proper perspective during the various stages of the curriculum. In practical work and in reading, every student should examine his methods of study periodically, ruthlessly scrapping unprofitable habits and customs.

READING AND PRACTICAL WORK

Walker believes that reading should be done in the evening. The student should consider the technic of reading. At the outset, the student should decide whether he remembers best by merely looking at a written word, by writing it down or by hearing it spoken. That is, he should learn whether he has a "visual memory" or an "auditory memory." The former fortunately is more common. Every student must investigate his powers of memory by actual experiment, decide his own classification, and work on it. Once the most favorable channel for the reception of facts is decided, the details of study can be regulated. Study from books should be done in privacy in an environment conducive to alertness and clarity. Anything conducive to too much physical comfort must be shunned. No attempt should be made to read soon after a meal or when tired. Reading in the train or bus or "at any old time" is a waste of energy and promotes staleness. As a general rule, it is said that, if the practical work of a working day has been faithfully performed, two hours' book work in the evening is ample. It is then that reading should consolidate and fix the practical work done during the day.

Walker believes it should be an inviolable rule that whatever has been seen or heard in the lecture room, laboratories or wards during the day should have first claim on the time available for reading during the evening. Surgery must be read during the performance of surgical appointments, ophthalmology while the student is actually seeing ophthalmic patients, and so on. It is worse than useless to attempt to acquire the formal dogmas of medicine by suddenly beginning at page 1 in a large textbook. The greater part of each morning and afternoon should be devoted to practical work and training. The surpassing value of dissection, of study in the wards, outpatient department and receiving room, of lectures which flavor facts with a lecturer's personal experience, and particularly of the "writing up" of patients' records, needs no emphasis. It may be taken for granted that a "part" once thoroughly dissected is etched deeply in the memory. Similarly, a scientific or clinical investigation once thoroughly per-

1. Walker, G. F.: *The Technic of Study*, *Lancet* 2: 481 (Aug. 31) 1929.

formed repays the investigator many times over by conferring ineradicable knowledge. In dissecting, the student should display the region so that he can subsequently recall it in three dimensions. And in investigating patients, when once the full straight facts have been clearly displayed, the imagination should be invoked to illuminate the patient's own side of the problem. For the precise and formal extraction of data about a patient, there is no more pithy and significant advice than the exhortation "Look and see." The cultivation of sincerity and the preservation of an ever open mind should be comprised in that advice.

The technique of practical study needs as much watchful care as does the technique of reading. It is very easy during the clinical years to be in a place where work can be done, should be done, and is in fact being done—by others. The tendency to lapse into intellectual somnolence during demonstrations is insidious in its onset, but a habit of vigorous enthusiastic attention is not difficult to acquire and when once acquired is seldom lost. The mere acquisition of the habit is worth while for its own sake; its utility will probably outlive the utility of many of the topics to which it is first applied. A large teaching hospital usually abounds in places where dawdling is possible and prevalent.

Here are two little pieces of advice. First, the midday meal should be taken free from "shop." Secondly, the notebook is worth consideration—a good small loose-leaf notebook should accompany the student through his whole curriculum. It should be just small enough to fit in the pocket, it should be available at all times, and each night it should be tidied up and full pages withdrawn to be placed in appropriate accumulations.

THE COURSE AS A WHOLE

The really fundamental thing to grasp is that the course is a whole, and not a string of loosely connected segments each requiring a concentrated onslaught with subsequent relegation to the background. I do not mean, Walker says, that a student should attempt to go forward three steps at a time but that he should look on his curriculum as a series of phases of initiation into the science and art. Each phase prepares the student for subsequent phases but is very dependent for its full consummation on preceding phases. To reduce this to practical terms it may be said, for example, that anatomy and physiology should forthwith be continuously studied during clinical work.

It follows from the fact of the unity of the course that the textbooks of each phase should be retained and kept viable during subsequent phases. Revision and maintenance of knowl-

edge is safer and easier if done from the actual pages of the big textbook used during the phase when it was intensely studied. "I say big textbook, because one big textbook should be selected for each topic and adhered to from start to finish. The small summaries and cram books have their place, but they are mainly useful as a help to marshal facts. The author of a most successful synopsis, far from making the usual claim to be meeting a 'long-felt want,' says in his preface that ultimate reliance on anything but the larger books will lead to failure. Just as the textbooks of successive phases should be carefully retained throughout, so must the microscope not be sold. I do not mean that the shelves should be laden with large textbooks on the history of medicine, but the bald facts of study can be enlivened by reference to an encyclopedia when a proper name is found. And from time to time monographs should be perused."

EXAMINATIONS

It is useless to ignore the fact that examinations loom large in the curriculum. "I have many times told my student friends that the examination incidents—and I am convinced that 'incident' is the right word—should be happy episodes. This information has always evoked incredulity, but on several occasions graduates have subsequently admitted personal verification. Of course, only fools make light of examinations. They should be taken so seriously that the student, as soon as he enters a particular phase, should plan his work for the terminal examination of that phase by actual time-table and schedule. He should record diagrammatically his progress through the phase so that the work is spread evenly over the time available. As an example let us suppose that a phase of study in one of the ancillary subjects lasts six months and that the textbook concerned has 500 pages. Then 100 pages must be covered each month by schedule, the actual pages being selected each evening according to the nature of the particular lecture, demonstrations and practical work enjoyed during the day. The art of passing examinations consists in doing steady comprehensive work during the whole of the antecedent phase. He who works steadily in the practical work of a phase with concurrent systematic reading cannot be 'plowed.'"

BRIEF REST PERIODS

It may be practical to review the psychological data whose interpretation may facilitate study, as has been done by Gillespie² at Guy's Hospital in London. It is found, he says, to be beneficial

2. Gillespie, R. D.: The Art of Study: Its Principles and Their Application, Brit. M. J. 2: 365 (Sept. 1) 1928.

if brief rest pauses are introduced at intervals during long periods of work. Thus not only may mental work be made more efficient but the output of factories has been favorably influenced. It is usually considered that to transfer one's attention to another task after feeling fatigued at a previous one is efficacious in restoring mental efficiency. The so-called "subjective fatigue," which is another name for boredom, tends to be abolished in this way. Mental fatigue is a matter of comparative unimportance. Only a small part of it is probably attributable to cerebral activity, and even this part is readily abolished by a rest pause or by normal periods of sleep. The greater part of mental fatigue is made up of boredom or by the so-called "specific objective fatigue," which is surmounted by changing over to another type of mental activity. The apparent mental incapacity in cases of "mental exhaustion" is nearly always the result not of intellectual effort but of anxiety or some other emotional disturbance, resulting from preoccupation with some personal problem. This is dramatically illustrated in the sudden recovery of persons complaining of "brain-fag" which has perhaps limited their work to periods of less than an hour each, when a source of worry is removed. Gillespie says that for practical purposes the mind is almost tireless. Even when there is considerable deprivation of sleep, intellectual work may be persistently maintained at a high level if the worker does not worry about his insomnia.

OUTSIDE INTERRUPTIONS

There is a factor called "warning up" that occurs as the task proceeds. Our mental machinery seems to have a degree of inertia which can be overcome only gradually. Hence the importance of avoidance of outside interruptions. To be called away to a telephone causes a greater loss in efficiency than is indicated by the mere loss of time; the amount of work done immediately after such an interruption is less than the output immediately before the interruption. It is desirable, therefore, to arrange work in such a way that it can be carried on without interruption for several hours at a time if need be. Much of the most difficult part of a difficult study is the beginning of it. A careful arrangement of very brief rest pauses will increase the total mental output, but the distribution and length of the pauses have to be worked out empirically by each individual for the type of work that he does.

Memory is one of the most important aspects of the mental process involved in study, but mere memory in the sense of physiologic retentiveness is not enough. To have it in a high

degree is an asset, but unless its stores are usable in an intellectual way a phenomenal memory may even be a hindrance. The author cites an experiment which seems to show that the last night's cram before an examination is of little benefit unless for the acquisition of entirely new material. We lose only slightly by abstaining from all work in the last few days before an examination and probably gain considerably in that elusive quality called "freshness."

In merely learning anything by heart, certain devices are of value. Grouping the material to be learned into intelligible unities naturally occurs to every one; presence of rhythm makes learning easier. It is easier to learn poetry than prose. It has also been found experimentally that, if a poem of several verses has to be memorized, it is more economical in the long run to learn it as a whole rather than stanza by stanza. We remember best what interests us most. Interest reduces also the effort both of attention and of remembering, and it increases the powers of observation as well. Interest leads also to selection and under its influence we select what we wish to remember often without realizing it.

But not everything, Gillespie says, should be left to this instinctive selection. With some people there is too much slavish routine reading, too much of plowing through masses of perhaps unnecessary and irrelevant textbooks, omitting nothing lest anything be missed, as some people read every page even of the inferior works of fiction produced by a good author.

MEMORIZING

There is no evidence for the statement, sometimes heard, that everything seen or heard or done is retained and that nothing is ever completely forgotten. Consider what would happen if we did not, practically at least, forget much of our experience. In recalling some event we would revive the smallest details and its recollection would require as much time perhaps as the event itself, and thus we would hardly have time available to register new impressions. Memory then is selective. The best memory is possessed by the man who makes the greatest number of associations with his experience; but the most effective memory is a combination of associative richness with selection. The man who thinks about his experience has much the better memory, and this marks the distinction between crammed information and real knowledge of the subject.

There are methods whereby association can be multiplied, and some of them are by discussion and debate and by reading different books in the same field, and also by writing

about the subject. Writers of textbooks and monographs frequently acknowledge that the persons to whom the writing has been most beneficial has been the authors themselves. It is not possible to write about every topic while preparing for an examination. A valuable exercise is the writing of papers; and they need not be necessarily on original work. It is good for the student to read regularly one of the current general medical periodicals, together with occasional issues of the more specialized journals. After graduation, the first few years often have to be spent by the young medical man in ridding himself of the unquestioning faith in authority and in the printed work that he has acquired during the student days, and of the parrot-like habits of memorizing rather than understanding.

The methods of study adopted must vary with the individual and with the nature of the subject. Some stress the regularity of habits of study, as a habit can thereby become established which has a certain dynamic effect of its own.

INCENTIVES TO STUDY

The subject "Incentives to Study" came to the attention of the Yale University student body a few years ago and found expression in a survey. A questionnaire was sent to each undergraduate and about 50 per cent of the total student body returned answers. Reviewing the summaries of this survey, Davis³ reaches the following conclusions: (1) Definiteness and direction of purpose become incentives to study; (2) concentration, rather than distribution, should be the curricular desideratum; (3) superior motivation placed Yale's poorer students in the lead in scholarship, but excessive financial handicap may overcome motivation; (4) it is the student's belief that for honor men the two final college years should be wholly tutorial; and these tutors should be the greatest teachers, instead of such men being reserved for the large lecture courses.

PROCESS OF STUDY

The following steps in studying any definite section of a subject are suggested by Ryerson of the University of Toronto: (1) collection of data, (2) selection and organization, (3) assimilation.

Data may be collected by the student from any source available. Selection and organization involve judging and condemning so-called facts, then dividing ideas into groups. Deductive reasoning descends from the general to the particular, while inductive reasoning separates the relevant from the unimportant. Safety and skill in neglecting some and accepting other

facts may be developed by proceeding from the principal thoughts to the details. The central idea must be found and firmly gripped. Principal thoughts must be searched for and recalled frequently for valuation. All articles should progress by groups of facts.

Assimilation is getting nutriment into usable form to accomplish a purpose. Ideas are recalled by their relation or connections with other ideas.

Individuality must be realized, the power to work must be developed, and system should be cultivated. Concentration of attention is to be acquired to eliminate waste.

MEDICAL PRACTICE OF THE FUTURE

What is it that leads men to enter the medical profession? In most cases the modest goal is that of earning an honorable living. Some cherish the ambition of contributing to the advancement of medical science, others the still loftier aim of serving their fellow men. An astute minority strives for personal aggrandizement and for the all too rare distinctions allotted to medical men. Whatever our initial impulse may have been, we have embarked on a swiftly flowing stream with many currents and hidden rocks. We should realize these hard facts. Considering all the circumstances of its past environment, the products of our orthodox system of education have been wonderfully good. Tradition is sometimes a valuable stimulus; on the other hand, it may act as a drag on imagination and progress. Under our present social and educational régime, an increasing proportion of bright young men and women throng our higher schools and universities, and in due course they swell the crowded ranks of the medical profession. Graduates are now turned out by mass production, more or less standardized and polished, like motor cars belonging to a particular factory and, like motor cars, tending to become out of date when compared with later models.

The young graduate, once he has secured his diploma of proficiency, usually has a transient wave of optimism. He soon discovers that he has fallen out of the frying pan of undergraduate life, even if supplemented by post-graduate experience, into the fire of everyday practice with new responsibilities and anxieties. He finds that the environment and equipment required for successful family practice are utterly different from the hospital conditions in which he has been trained. This is not strange, since few of his teachers have been through

3. Davis, James E.: Teaching and Learning, J. Michigan M. Soc. 35: 311 (May) 1936.

Abstract of an address delivered by Sir James Purves-Stewart before the University of Leeds Medical Society, Edinburgh M. J. 45: 309 (May) 1938.

the mill of general practice. The common diseases for which he is now consulted are unlike those dramatic clinical pictures on which he concentrated his attention in hospital wards and theaters. He comes to realize the truth of the aphorism that "there is no such thing as a disease; there is only a sick person," and that his success largely depends on studying and dealing with the personalities of his patients.

His primary problem is usually economic. A few lucky young graduates find comfortable practices awaiting them. The more brilliant students may be attracted to teaching or to research; others may undergo further training with the intention of qualifying as specialists. The majority are content if they can find congenial employment and economic independence. Even in England the supply of medical graduates is already becoming greater than the demand, although in this respect we compare favorably with some other countries. In Germany the proportion of medical men has become so high that the average graduate has to wait some ten years before he succeeds in attaining an independent practice. In France the proposal has recently been made that all medical men on attaining the age of 65 years should be compulsorily retired, they being treated as crumbling monuments. The economic problem is becoming increasingly anxious. And yet, after all, to the man of scientific mind, even when his own personal problem of earning a living is successfully solved, this is only the working foundation of his career.

Each generation of medical graduates differs from its predecessors. Until the middle of the nineteenth century, and later, every qualified practitioner was regarded as a completely equipped medical unit, a walking compendium of knowledge, able to attack any problem presented to him by his trustful patients. But since those days of the so-called all-round man, not only has the pace quickened but the load to be carried has become heavier.

The first stage of specialism in modern clinical work was when general or major medicine diverged from general or major surgery.

THE SPECIALTIES

The specialties within the medical profession are steadily increasing. The laboratory worker, the biochemist, the radiologist, the pharmacologist and others now perform work that is indispensable to the clinician, who has neither the special knowledge, the instrumental equipment nor the technical dexterity requisite for carrying out such observations. Secondly, there are the clinical specialists, who confine their activities to one special organ, or to one special

aperture of the body. Their field is sometimes so restricted that they frankly admit being incapable of dealing with ailments outside it. Imagine a modern ophthalmologist supervising an obstetric case or a dermatologist dealing with a compound fracture. And the gallant general practitioner is expected by the public to deal successfully with all such cases. Nevertheless we need the skilled ophthalmologist and the expert dermatologist.

Specialism is advantageous, but in modern medical specialism there are dangers. One is the tendency of the specialist to lose the proper perspective of the patient as a whole. Another is the difficulty of keeping open the lines of communication between specialist and general practitioner. These lines daily become longer and more tortuous. When the vocabulary of any specialty becomes unintelligible to the average medical intelligence, it is in danger of losing its usefulness.

There are two kinds of specialists: the real and the false. Of the pseudospecialists there are examples to be found within the medical profession itself and a still more luxuriant crop of unashamed quacks outside it. He extends his practice mainly by astute canvassing. He has been deservedly pilloried by candid novelists. The pseudospecialist, greedy of notoriety and financial gain, is neglectful of ethical standards and sometimes actually dishonest. We are unhappily familiar with the blatant commercially minded consultoid who performs unnecessary operations on his richer patients for purposes of revenue and on his poorer ones in order to improve his technique. Sometimes he operates in order to accumulate and publish statistics demonstrating his own preeminent skill.

The true specialist is a man possessed of natural aptitude who, after intense training on special materials, sometimes necessitating dexterity in the manipulation of complicated apparatus, gradually attains to such a degree of knowledge and skill that he is deservedly recognized as a guide in difficult and doubtful problems. We have the good fortune to possess many such men.

How are we to recognize the true expert? He has characteristics by which he can be recognized. We observe the readiness with which he submits his results to control, criticism and reobservation by his colleagues. He records his negative results or failures as scrupulously as his successes. He avoids quoting so-called percentages when dealing with short series of figures. The pseudo-expert who has had four or five successful cases claims "100 per cent"

of successes. No one should speak of a percentage until he has had at least a hundred cases from which to quote.

What will be the future of medicine and of specialism? Every medical practitioner must remain a student to the end of his professional career. The day that a medical man ceases to learn, that is the day on which he should retire from practice.

THE FUTURE OF MEDICINE

Some practitioners may for a time succeed in remaining up to date, but after years of busy practice many of us would make a poor show at a professional examination, in competition with our juniors, or even with some of our own pupils. The standard of knowledge of the general practitioner of today often surpasses the peak of certain specialists twenty-five years ago.

It may seem impracticable to make all doctors attend from time to time graduate courses in medicine, surgery and therapeutics. Some of the best men in the profession do so. It is encouraging that a program of this sort has recently been presented by the Ministry of Health as a gift to general practitioners wise enough to take advantage of it. But so long as graduate courses are optional and not compulsory it is chiefly the best type of practitioner who will attend them, while the more obsolescent types will continue to plod along the old roads, obstructing the speedier models which overtake them on the journey.

The family doctor who studies not only the disease but also the patient, who knows his patient's personal circumstances and constitutional tendencies, can never be replaced by the red-tape government official. His level of scientific culture will continue to rise and his functions will become not less but more important. To him it will fall to make the clinical application of scientific advances in the prevention and treatment of disease.

True specialism is essential to the progress of scientific medicine. The specialist of the future, with his superior skill in a restricted field, may expect to continue to be paid on a somewhat higher scale than the general practitioner, but not disproportionately high. This discrepancy will tend to diminish as the specialist finds himself in company with his fellow workers, becoming a cog in the complicated machinery of modern social life.

The leaders of the medical profession in the future will not be drawn almost exclusively, as at present, from its professorial and specialist members. The cultured general practitioner will come increasingly to the front. He will be the natural leader in every health campaign. He will represent his colleagues and his patients.

He will defend their interests with a greater understanding than that of the academic members who now so largely comprise most of our official and deliberative assemblies.

THE DISCOVERY OF HENRY PLUMMER

In the year 1900 Dr. William J. Mayo¹ was called to Racine, Minn., in consultation with Dr. Albert Plummer to see a patient. Dr. Mayo drove the twenty miles from Rochester to Racine to find Dr. Plummer ill in bed. His son Henry, however, who had recently graduated, was in practice with his father and gladly went along to see the patient. The interesting story of this consultation is related here almost entirely in Dr. Mayo's own words. It was arranged, he said, that "I should leave my team of horses and ride the seven miles with Henry, who came out carrying a microscope. During the ride Henry talked to me about the blood, and he had an extraordinary amount of information about its composition, its characteristics and function, much of which I realized was not to be found in print at that time.

"The case we were to see was one of leukemia, of the type at that time called aleukemic leukemia; it is now designated leukopenic leukemia. Henry took a drop of blood from the ear of the patient, put it under the microscope and demonstrated the findings to me. He called in the hired man and a member of the family and took blood from each of them and under the microscope contrasted it with the blood of the patient for my information. On the way back he continued to talk about the blood, and spoke also of his interest in the thyroid gland.

"When I got home that night I told my brother that Dr. Plummer had a son in Racine who certainly knew more about the blood, at least, than any one I had ever met. I thought he was an extraordinary young man, and I believed we ought to try to bring him here and add him to the staff to bring our laboratories up to date. I wrote young Dr. Plummer and asked him to come up to talk with us. He came, we went over the situation, and he came on the permanent staff early in the year 1901.

"Henry took charge of the laboratories, and as a result of his efforts in a few months we possessed as good laboratories, I believe, as far as relation to clinical medicine was concerned, as were to be found elsewhere. In developing the laboratories he always kept the patient in mind. He used scientific apparatus not to take the place of clinical observation but to aid and verify.

1. Mayo, W. J.: The Work of Dr. Henry S. Plummer, Proc. Staff Meet., Mayo Clin. 13: 417 (July 6) 1938.

"I remember well that Dr. Charlie and I had been greatly impressed with the x-rays and such related mechanisms as were available at that early date, and we had acquired a rather imposing electrical machine. No one knew just what it could do, but it was thought to have some important diagnostic value. Unfortunately machines of this type were sometimes being used by charlatans to impress patients and for that reason we had all the connections of the machine which could be used for spectroscopic action pulled out and replaced with wooden pegs. We showed this machine to Henry, who was much amused. As he had developed the clinical laboratories, so he took over the x-ray work, and to the day of his death he carried the scars of x-ray burns on his hands.

"In 1889, when St. Mary's Hospital was first opened, in one of the earliest operative cases there was the largest thyroid tumor I have ever seen. The patient, a Scotchman aged about 62, lived near Racine, the home of the Plummer family. The patient had great difficulty in breathing and I knew that, whatever happened, the tumor must come out. While the patient made a good recovery, this was the beginning and end of my work in the goiter field.

"Henry Plummer as a boy knew this patient while at Racine and was familiar with the details of the case. It made such an impression on his mind that he became interested in the thyroid gland and in his college course followed the cases of thyroid disease in the dissecting room and the experimental laboratories. He remained intensely interested in the subject of the thyroid all his life.

"When Henry joined the staff, he was at once struck with the whole question of the purpose of the thyroid gland, its secretion, and its relation to health and disease. He made a special study of disturbances of function of the thyroid and cleared up many of the previously confusing ideas on the subject of thyroid disease. His studies on the effect of iodine in the pre-operative treatment of exophthalmic goiter led to an immediate reduction of the operative mortality in this disease to less than 1 per cent, and the necessity for multiple stage operations was almost eliminated. This elucidation of the role of iodine in the treatment of exophthalmic goiter ranks among the great contributions to medicine.

"The many papers Henry Plummer wrote showed the progressive bent of his mind. He assiduously attended meetings of medical societies for the purpose of gaining information as well as to contribute. Always he concentrated on the fundamentals, the blood, the circulation, the heart, the kidneys and their relationship to the thyroid gland and other glands of internal secretion. Look over the bibliography of his scientific publications. Each article was care-

fully prepared; each carried the work discussed a step further. For thirty-six years there was a continuous development of the subject to which he gave his life.

"In 1899, as chairman of the Section on Surgery of the American Medical Association, I had written my address on esophageal stenosis. In one case of a different type, the obstruction was almost complete, yet there was no history of a cause. I had made a gastrostomy and had discovered that I was able to pass a sound up from below. Henry took over the case, developed the theory of cardiospasm, brought about dilatation of the stricture by the use of esophageal sounds, and cured the patient. He continued in this field with the greatest enthusiasm and developed mechanical methods of removing foreign bodies from the esophagus. From this phase of the study he passed to the investigation of diverticula of the esophagus. He developed bronchoscopy for the removal of foreign bodies in the bronchi, accomplished dilation of bronchial strictures, and worked out the method of diagnosing disease conditions of the lung by securing specimens of involved lung tissue for microscopic examination. His study of oxygen requirements led to the building of airtight glass oxygen chambers. These rooms, which preceded the oxygen tents commonly employed today, are still in use. In this field he achieved extraordinary results. Henry was a genius in mechanical detail. The first Mayo Clinic building, begun in 1912, was essentially his work, in which the architects gratefully acknowledged his leadership. The present clinic building connected with the old is his monument.

"Loved by his confrères and respected by the learned men of the profession the world over, Henry S. Plummer passed away Dec. 31, 1936, at the age of 62. When stricken with bulbar paralysis he recognized what it was and asked to have the family summoned, saying that in an hour he would be unconscious. As long as that intelligence which had carried him through life was permitted to function, he traced the progress of this last illness.

"The life of Dr. Henry S. Plummer was devoted to the welfare of mankind."

How to Become a Diagnostician

The high-developed clinician examines his patients carefully and minutely, he recalls the course of disease in past patients and becomes a prophet of the future course of disease in each new patient; he knows from experience the possibilities and the failures of treatment; he is cool and collected; he plans a campaign of therapy and pursues it day by day, not easily driven from his plan unless new conditions develop. . . . Persistently experience and knowledge are increased; eventually by reason of attainment in experience and knowledge increasingly the physician is sought by other physicians for help in solving their problems; he has become a consultant.—Christian, Henry A.: *The Lure of Medicine*, *Virginia M. Monthly* 65:515 (Sept.) 1938.

Medical College News

Medical schools, hospitals and individuals will confer a favor by sending to these headquarters original contributions, reviews and news items to be considered for publication in the Student Section.

Interns' Contest in Mahoning County, Ohio

Four interns presented case reports before the Mahoning County Medical Society in Youngstown, Ohio, June 21, at the annual Interns Contest sponsored by the society. The first prize of \$15 was awarded to Dr. Densmore Thomas for his paper on "Trichinosis" and the second prize of \$10 to Dr. Donald A. Miller for his report of a case of "Stab Wound to the Left Side of the Chest." The prizes were awarded in consideration of the completeness of the work-up of the case, the significance and teaching value of the case itself, and the manner of presentation. The four papers were so equally interesting that the decision of the five judges was reached on the delivery alone.

Memorial in Africa to Noguchi and Young

A memorial to the late Drs. Hideyo Noguchi and William Alexander Young was formally unveiled by Sir Arnold Hodson at Akkra, Gold Coast, Africa, April 2. A representative gathering of the people of Akkra was present at the ceremony. Before the unveiling Dr. David Duff, director of medical services for the Gold Coast, gave an account of the work of these two medical martyrs. In addition to this memorial a brass plate, suitably inscribed, will shortly be placed in the room of the Medical Research Institute at Akkra, where Noguchi and Young conducted their yellow fever studies. Noguchi had gone to the Gold Coast in British West Africa as representative of the Rockefeller Institute for Medical Research, New York, to complete researches on yellow fever, and he died of that disease at Akkra, May 21, 1928. He was born in Japan and graduated in medicine at Tokyo Imperial University in 1897. Subsequently he worked in the University of Pennsylvania. Young, also one of a scientific party sent to Akkra by the Rockefeller Institute for Medical Research, died there May 29, 1928, of yellow fever. Dr. Young was of Scotch descent and received his medical education in England.

Fellowships Available in Chile

Two fellowships will be available next year to American students for study at the special January session of the University of Chile. These fellowships are offered by the Chilean government and include tuition, 900 Chilean pesos for living expenses, and a pass on the Chilean railroads. In addition the Carnegie Endowment for International Peace has granted \$500 to each fellowship to cover traveling expenses to and from Chile. Preference is given to candidates who have had at least a year of graduate work. Applications are available at the Institute of International Education, 2 West 45th Street, New York City.

Hunterian Professorship Awarded to Canadian

The Hunterian professorship in the Royal College of Surgeons of England has been awarded to Dr. Donald W. G. Murray of Toronto. This is the second time this award has been given to a Canadian professor, the other occasion being in 1924, when Dr. William E. Gallie of Toronto was so honored. The distinction comes to Dr. Murray as a result of his work on heparin, which has been done in conjunction with Dr. Charles H. Best, professor of physiology of the University of Toronto. Dr. Murray will give his lecture in London, England, next year.

Fiftieth Anniversary of Marine Biological Laboratory

The fiftieth anniversary of the Marine Biological Laboratory, Woods Hole, Mass., is being celebrated this year, according to *Science*. A portrait of Mr. Charles R. Crane, New York, who was largely responsible for the growth of the institution, was presented at an informal meeting to celebrate the semicentennial of the laboratory. Mr. Crane was president of the board of trustees from 1902 until 1925; he gave a completely equipped laboratory building in 1914 and later a large sum for an endowment fund. The first building was opened for the use of seven investigators and eight students in the summer of 1888, with Prof. C. O. Whitman, Chicago, as director. The attendance is now more than 500. To the original building, still used for investigation and research, have been added other wooden buildings and a large brick laboratory containing a library, research rooms equipped with running fresh and salt water, chemical and apparatus rooms, an x-ray installation and a large auditorium. A statement of Professor Whitman expresses the aim of the laboratory: "The Marine Biological Laboratory attaches itself to no single institution but holds itself rigidly to the impartial function of serving all on the same terms. . . . The whole policy is national in spirit and scope. The laboratory exists in the interests of biology at large." Recent changes in the staff include the appointment of William W. Ballard, Ph.D., assistant professor of zoology and anatomy, Dartmouth College, Hanover, N. H., and Douglas M. Whitaker, Ph.D., professor of zoology, Stanford University, California, to succeed Lester G. Barth, Ph.D., assistant professor of zoology, Columbia University, and Charles Packard, Ph.D., assistant professor of zoology at Columbia, who resigned from the embryology staff.

Faculty Changes at Oklahoma

The University of Oklahoma School of Medicine, Oklahoma City, has conferred the title of emeritus professor on Dr. Edmund S. Ferguson, professor of ophthalmology; Dr. William M. Taylor, professor of pediatrics, and Dr. John F. Kuhn, professor of gynecology. Dr. Leslie M. Westfall, professor of clinical ophthalmology, succeeds Dr. Ferguson; Dr. Clark H. Hall, associate professor of pediatrics, succeeds Dr. Taylor, and Dr. Grider Penick, associate professor of gynecology, succeeds Dr. Kuhn.

Vermont Now Requires Three Years for Admission

The College of Medicine of the University of Vermont has adopted requirement of three years of college work as minimum for admission. This will take effect next fall.

Miss Helena McMillan Retires

Miss Helena McMillan, a leader in hospital and nursing education and for thirty-five years head of the School of Nursing of the Presbyterian Hospital of Chicago, has announced her retirement as director of that school effective in October. Miss McMillan's work has not been confined to nursing; she has been interested also in hospital administration and the development of better care of the sick in the home as well as in the hospital. The *Journal of the American Hospital Association* points out that she is perhaps the only

person living who participated in the second annual convention of the American Hospital Association in Cleveland, at which time Miss McMillan presented a paper on "The Relationship Which Should Exist Between the Superintendent of the Hospital and the Superintendent of Nurses." Miss McMillan was at that time superintendent of the School of Nurses of the Lakeside Hospital in Cleveland.

Ohio Personals

Dr. Alec Laidlaw Phimister has resigned as demonstrator in medicine at Western Reserve University School of Medicine in Cleveland to enter the practice of medicine in London, England. Dr. Kenton R. Phelps, graduate of Western Reserve University School of Medicine in 1935, was appointed a resident in neurologic and cardiac surgery at the University Hospitals, Cleveland, beginning July 1, 1938. Dr. Carl H. Lenhart, director of surgery in the University Hospitals of Cleveland, has been elected president of the Cleveland Medical Library Association. In addition to being professor of surgery at Western Reserve University School of Medicine, Dr. Lenhart has been "directing librarian" for eighteen years.

Alumni Reunion in Ann Arbor, Mich.

A reunion of the alumni of the University of Michigan Medical School and of the former staff members and interns of the University Hospital, Ann Arbor, was to be held September 29-October 1. Among other speakers were the following:

- Dr. Reuben Peterson, Duxbury, Mass., Landmarks in the History of the University of Michigan Medical School and Its Hospital.
- Dr. Cyrus C. Sturgis, Ann Arbor, A Résumé of Eleven Years' Experience in Hematology at the Simpson Memorial Institute.
- Dr. Donald D. Van Slyke, New York, The Physiology of Renal Excretion.
- Dr. Norman F. Miller, Ann Arbor, Common Lesions of the Cervix.
- Dr. Ward J. MacNeal, New York, Bacteriophages as Aids in Dealing with Infections.
- Dr. Carl E. Badgley, Ann Arbor, A Study of the Causes and Methods of Prevention of Nonunion of Fractures of the Shaft of the Long Bones.
- Dr. Walter Bauer, Boston, The Physiology of Normal Joints and Its Relation to Joint Disease.
- Bradley M. Patten, Ph.D., Ann Arbor, The First Heart Beats and Circulation of Blood as Shown by Micro Röntgen Embryos.
- Dr. Joseph Brennemann, Chicago, The Intrinsic Factor in the Inheritance of Retinoblastoma.
- Dr. Joseph Brennemann, Chicago, Abdominal Pain in Children.
- Dr. Hugo A. Freund, Detroit, Renal Ischemia and Vascular Hypertension Associated with Coarctation of the Aorta.
- Dr. Max M. Peet, Ann Arbor, Results of Splanchnectomy for Hypertension.
- Dr. Hugh Cabot, Rochester, Minn., Intravenous Urography: Its Place in General Medical and Surgical Diagnosis.
- Dr. Francis E. Seneear, Chicago, The Serologic Diagnosis of Syphilis.
- Dr. Frederick A. Collier, Ann Arbor, Physiology and Chemistry in Surgery.
- Dr. Frank N. Wilson, Ann Arbor, The Differential Diagnosis of Coronary Occlusion.
- Dr. Charles W. Edmunds, Ann Arbor, The Problem of Drug Addiction.
- Dr. Warren T. Vaughan, Richmond, Va., Tissue Tension Studies in Clinical Allergy and Experimental Anaphylaxis.
- Dr. James B. Herrick, Chicago, Acute Endocarditis.
- Dr. Louis H. Nephew, Ann Arbor, A New Interpretation of Diabetes Mellitus in Normal and Obese Persons.
- Dr. Perrin H. Long, Baltimore, Further Observations on the Experimental and Clinical Use of Sulfanilamide.
- Dr. Frederic M. Loomis, Oakland, Calif., The Third Component: The Relationship Between Them.
- Dr. Hiram Winnett Orr, Lincoln, Neb., Methods for the Prevention and Cure of Septicemia Following Injuries and Surgical Operations.
- Dr. Udo J. Wile, Ann Arbor, Sex Hormone Studies in Aene. The Urinary Excretion of Androgenic and Estrogenic Substances.

Dr. Frederiek G. Novy, dean emeritus of the medical school, was the speaker at the banquet in the Intramural Sports Building. Dr. Bauer and Dr. Richard H. Freyberg, Ann Arbor, conducted a round table discussion on arthritis at a luncheon September 29. The following day a symposium on poliomyelitis was pre-

sented at luncheon. The reunion was to be concluded October 1 at the opening convocation of the medical school when Dr. Francis Peyton Rous of the Rockefeller Institute for Medical Research, New York, was the speaker.

Aid for Study of Vascular Problems

The Taylor Instrument Companies, Rochester, N. Y., gave \$5,000 to further investigation in the field of vascular problems by Drs. Mont R. Reid and Louis G. Herrmann of Cincinnati. This gift will be placed in the Pavaex Appreciation Fund. According to the *Journal of Medicine*, Drs. Herrmann and Reid have given years of altruistic endeavor in their development of passive vascular exercise therapy, and the Taylor Instrument Companies has manufactured the instrument without financial profit. Dr. Reid is head of the department of surgery, and Dr. Herrmann is assistant professor of surgery and director of the vascular clinics at the Cincinnati General Hospital.

Promotions at Vanderbilt

The following promotions at Vanderbilt University School of Medicine, Nashville, have been approved by the board of trustees: Dr. Samuel M. Bloomstein to professor of clinical pediatrics, Dr. Leonard W. Edwards to associate professor of clinical surgery, Dr. Rudolph H. Kampmeier to associate professor of medicine, Dr. Ralph M. Larsen to assistant professor of surgery and anatomy, and Dr. Guy Sydney McClellan to assistant professor of obstetrics and gynecology.

Aid for Pellagra Investigation

The Markle Foundation, New York City, has appropriated \$14,000 to support the investigations of pellagra for a two year period now being conducted by Dr. Tom D. Spies, associate professor of medicine at the University of Cincinnati College of Medicine. The Josiah Macy Jr. Foundation gave \$4,500 to support these investigations until next February.

Prizes for Students at Maryland

A prize of \$25 is given each year by Mrs. Abram B. Gailther, as a memorial to her late husband, to the student in the senior class at the University of Maryland School of Medicine who does the best work in genito-urinary surgery.

Another annual prize of \$25 has been established by Mrs. S. M. Shoemaker and Mrs. B. F. Johnston as a memorial to Samuel M. Shoemaker for the best essay on "Milk in Relation to Public Health," written by a student in the senior class.

Pathologists Appointed at Long Island

Dr. Caspar G. Burn, assistant professor of pathology at Yale University School of Medicine, New Haven, Conn., has been appointed associate professor of pathology at Long Island College of Medicine. Dr. Burn graduated from Yale in 1930. Dr. John Musser Pearce, recently on the staff of the Rockefeller Institute for Medical Research, Princeton, N. J., has been appointed instructor in pathology.

Gift for Gynecology at Pennsylvania

The University of Pennsylvania School of Medicine has received \$50,000 from the estate of Dr. William C. Goodell, who died in 1918. The bequest is to establish the William Goodell chair in gynecology, it was reported.

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ERYSIPELOID AS AN OCCUPATIONAL DISEASE

CHAIRMAN'S ADDRESS

JOSEPH V. KLAUDER, M.D.

PHILADELPHIA

The skin disease which Rosenbach in 1884 designated erysiploid is now known to be an infection caused by *Erysipelothrix rhusiopathiae*, the organism of swine erysipelas. My previous reports¹ concerned the infection in swine and in human beings, especially commercial fishermen. The organism was recovered by culturing an excised piece of involved skin from swine and from patients. Bacteriologic studies, serologic reactions and the virulence of organisms recovered from different sources were reported.

My purpose now is a clinical analysis of 100 cases of erysiploid, with particular reference to the occupational nature of the disease. Eighty-eight of the patients were infected through an injury to the hands in the course of employment and were claimants under workmen's compensation laws. The infection is therefore of importance to the industrial physician.

THE ORGANISM AND THE INFECTION IN SWINE

It will suffice now to discuss briefly the organism and the infection in swine. There are three generally accepted strains, human, swine and mouse, although the organism has been found in a considerable assortment of animal species either as a harmless parasite or as the cause of disease. Its wide dissemination is extraordinary. It is found wherever nitrogenous substances are decomposing. In putrid material the organism is capable of retaining its viability and virulence for months. In certain environments it exists in the soil as a saprophyte.

The virulence varies considerably in different species and in the same species. The organism has a capacity to change suddenly from a harmless saprophyte to a pathogenic parasite. This transition occurs particularly in swine. Man is relatively immune, particularly when the organism enters through the gastrointestinal tract.

In human beings and swine the organism has an affinity for the skin. Pigeons and white mice are highly susceptible to artificial infection; rabbits and guinea pigs considerably less. Field mice are immune (a means of differentiation).

The virulence as well as the appearance of the organism can be modified by serial passages through animals and also by culture. Passage through rabbits increases the virulence for this species but decreases it for swine. Passage through pigeons increases the virulence for all animals. In our studies a three year old culture of a swine strain was no longer pathogenic for white mice and pigeons.

The infection is one of the most serious diseases of swine. It is manifested in three forms. A mild form ("diamond skin" disease), characterized by slight constitutional symptoms and the presence of sharply circumscribed quadrangular, bluish red lesions on the skin; a severe form, characterized by constitutional symptoms of septicemia, the presence of diffuse areas of erythema and at times vesicles, petechia and necrosis, and a chronic form, characterized particularly by polyarthritis (fig. 1) and at times symptoms referable to a vegetative type of endocarditis.

The disease in swine, long prevalent in Europe, has been increasing in the United States. It was first reported here in 1921 but there were only a few isolated cases until about 1930, when an outbreak was reported in South Dakota. Since that year the malady has appeared in practically all states.²

CLINICAL FORMS OF ERYSIPELOID

The disease in man as first described by Rosenbach was a mild, rather localized, cutaneous infection. This is the usual form of the disease and is later discussed. It is now known that the disease may, although rarely, be expressed as acute septicemia with a fatal outcome or as a generalized cutaneous infection with arthritic and constitutional symptoms, the arthritic symptoms predominating somewhat. The latter form is comparable to one form of the infection in swine.

The localized cutaneous form of the disease occurs at the site of epidermal defect on any part of the skin, usually the hands; it is of variable severity, with or without localized arthritic or constitutional symptoms. The first symptom is pain at the site of inoculation and is followed by swelling and erythema. The most distinctive feature of the disease, of considerable diagnostic import, is the purplish red color of the erythema. The erythema slowly progresses (figs. 2, 3, 4 and 5), producing another distinctive feature, a sharply defined, slightly elevated, zone (fig. 2), which extends peripherally as the central portion fades away. The involved

Read before the Section on Dermatology and Syphilology at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 15, 1938.

1. (a) Klauder, J. V.: Erysiploid and Swine Erysipelas in Man: A Clinical and Bacteriologic Review; Swine Erysipelas in the United States, J. A. M. A. 86: 536-541 (Feb. 20) 1926. (b) Klauder, J. V.; Righter, L. L., and Harkins, M. J.: A Distinctive and Severe Form of Erysiploid Among Fish Handlers: Report of Clinical and Laboratory Studies; Demonstration of the Bacillus of Swine Erysipelas, Arch. Dermat. & Syph. 14: 662-678 (Dec.) 1926. (c) Klauder, J. V., and Harkins, M. J.: Erysiploid in the United States: Clinical and Laboratory Study, J. A. M. A. 96: 1205-1209 (April 11) 1931. (d) Klauder, J. V.: Generalisiertes Erysiploid: Bericht über einen 29 Monate dauernden Fall mit Sektionsbefund, Dermat. Wehnschr. 98: 613-619 (May 19) 1934.

2. Hog Raisers Cautioned Against Swine Erysipelas, Press Service, U. S. Department of Agriculture, Washington, D. C., June 28, 1937.

area is swollen and tense, as though fluid had been injected intracutaneously. If the finger is involved the swelling and tenseness make movement difficult.

Another characteristic of the disease is its migratory nature; new purplish red patches appear at remote areas. If the infection originally involved one finger, eventually all the fingers and the dorsum of the hand or

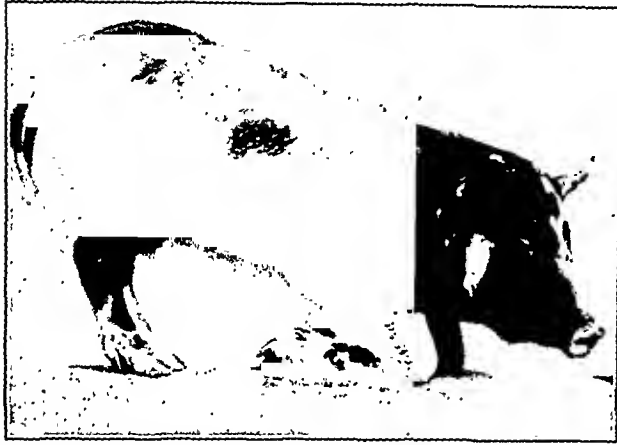


Fig. 1.—Acute arthritis with erysipelas infection in the swine. Note the swollen condition of the joints, particularly of the front feet, on which the animal refused to bear weight. (From the Bureau of Animal Industry, United States Department of Agriculture, Washington, D. C.)

palm (fig. 3) or both may become affected, the erythema appearing and extension may take place by continuous migration. The erythema may completely disappear at the areas first involved at the time other areas are affected. The disease involutes without desquamation.

The appearance is not that of a pyogenic infection, with which the condition is frequently confused. The color of the erythema is different, there is no pitting on pressure, and suppuration never occurs. Although itching and tingling are frequently present, pain is the most conspicuous subjective symptom. It is throbbing and burning in character, often preventing sleep. Other features of the disease are discussed in the analysis of cases.

The mildness or severity of infection usually suggests the source of infection; this in turn governs the virulence of the organism. In our studies infection was more severe when contracted from a fish source.³ The virulence of the organism isolated from this source was greater than that isolated from other sources.⁴ From our studies and from clinical observation it appeared that the organisms from the following sources, in the order stated, were the most virulent: (1) partly decomposed fish, (2) live slimy fish, (3) swine, (4) fish in the retail market and (5) other sources.

ANALYSIS OF 100 CASES

Sex.—Of the 100 patients, ninety-three were males. Of the seven females, four were employees in an

abattoir, one was a housewife who was infected while cleaning fish, one was a dressmaker and the remaining one a food handler.

Source of Infection.—The source of infection is evidenced in the occupation of the patient and is shown in the accompanying table. The predominant occupation was work in an abattoir (figs. 2 and 4).⁵ Infection among the employees of abattoirs was not confined to those engaged in slaughtering swine but affected employees handling all parts of the swine, including the bones and pork products. Men engaged in making sausages or scrapple or in handling lard or objects exposed to swine or swine products, such as machinery, boxes, crates and tables were infected. For example, one patient, a driver of a meat truck, cut his finger on the door, and erysipelas appeared at the site of injury. It is possible that in this and similar cases the organism was present on the soiled hands of the worker rather than on the object injuring the skin.

The next most frequent source of infection was fish. Of sixteen patients infected from this source eleven were engaged in cleaning fish for retail sale (fig. 3), one handled fish in his occupation, one was a housewife and three fished for pleasure and were infected at the site of a cut or puncture wound on the finger.

The student veterinarians were infected when dissecting a dead horse. The patients listed under the occupations connected with tallow and grease included men gathering scraps of meat, fat and bones from retail meat stores and men handling this material in making grease, tallow, fertilizer and chicken feed. The patient listed as a weaver cut his finger when handling wool, and no other source of infection could be determined from the history. The dressmaker pricked her finger when handling spangles on dresses; the source of infection could not be determined. Lard was apparently the source of infection in bakers. One patient,

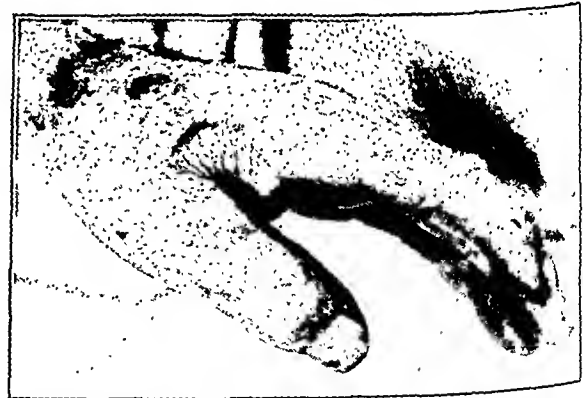


Fig. 2.—Erysipelas of eight days' duration in an abattoir employee who cut his thumb while working. Note the sharply defined and elevated border.

a boy, was infected by an opossum. He scraped his knuckles on a rock in the dry bed of a stream and later carried the animal by wrapping its tail around the injured fingers. The food handler, who filled glass jars with such food as India relish and potato salad, had infection appear at the site of a cut caused by a broken glass jar. Crabs and fish cooked at her place of employment were the probable source of infection.

5. In an abattoir in Philadelphia employing about 400 men, the yearly incidence of erysipelas among the employees was about 2 per cent during the past three years. Dr. Glenn S. Everts of Philadelphia supplied these figures.

3. There is no known disease of fish caused by the organism of swine erysipelas. It appears that the slime of the fish attracts the organism from refuse thrown into the water and other decaying matter and that change of environment increases the virulence.

4. The most virulent strain we isolated from a fish source killed white mice in four days after intraperitoneal injection of the smallest amount employed, 0.0000001 cc. of a forty-eight hour pure culture in hormone bouillon. This compared with the following lethal doses of a forty-eight hour pure culture of the organism from different sources injected subcutaneously into white mice: swine source, the most virulent strain studied, 0.001 cc. killed in five days; rabbit source, 0.01 cc. killed in five days; turtle source, 0.1 cc. killed in five days. Stickborn, quoted by Wilhelm Kolle and August Wassermann (Handbuch der pathogenen Mikroorganismen, ed. 2, Jena, G. Fischer, 1913, vol. 6, p. 12) gave 0.000001 cc. of a forty-eight hour bouillon culture of a swine strain of the organism as the lethal dose for white mice.

Injury.—Epidermal defect plays an important part in inoculation. There was a history of injury at the site at which the infection first appeared in all but five cases in this series. The injury consisted of a cut, puncture wound or abrasion. In one case infection appeared at the site of paronychia and in another at the site of an abrasion caused by cutting the cuticle

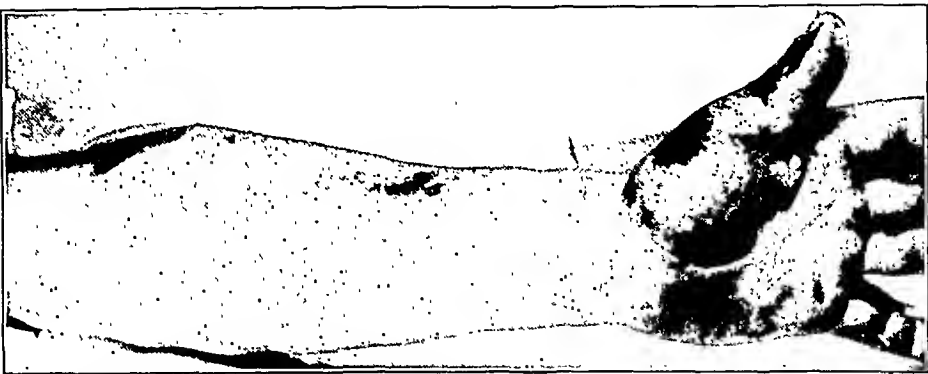


Fig. 3.—Erysipeloid of eight days' duration in an employee who was infected while cleaning fish. The fingers, hands and both surfaces of the forearm were involved. Immune serum (30 cc.) was injected intramuscularly, and the infection disappeared. There was no serum sickness. (The two wheals represent a negative test for sensitization to horse serum.)

too close. In nine cases infection occurred despite the application of alcohol, tincture of iodine or mercurochrome at the site of injury immediately or soon after its infliction.

Incubation Period.—The first symptom, usually pain, appeared within twenty-four hours in seven cases, in one day in twenty-four cases, in two days in nineteen cases and in three days in six cases.

Localization and Spread of Infection.—The hand was involved in all cases, and the infection invariably appeared first on one finger. In three cases both hands were involved. In five cases the infection was mild and remained localized in the finger involved. In all other

Source of Infection or Occupation of 100 Patients with Erysipeloid*

Abattoir	58
Fish, retail	11
Tallow, grease, fertilizer	7
Veterinary students (dissecting horse)	6
Butchers, retail	3
Fishermen, pleasure	3
Bakers (lard)	2
Clam opener	1
Food handler	1
Furrier (unfinished pelt)	1
Rabbit (removing skin)	1
Opossum (carrying animal)	1
Weaver	1
Dressmaker	1
Housewife (cleaning fish)	1
Fish (handling)	1
Kitchen worker	1

* Eighty-eight of these patients were infected through injury in the course of employment and were claimants under workmen's compensation laws.

cases the infection progressed, eventually involving different fingers and parts of the hand. The wrist became involved in thirteen cases and the forearms in six (fig. 3).

In one case, which I^{1d} have reported elsewhere, the entire cutaneous surface became involved. Infection started on the finger at the site of injury caused by a stale fish head used for bait. About five months later the infection spread beyond the wrist and gradually involved the skin of the forearm and arm. Despite all variety of treatment there was a gradual spread, and at the end of a year the entire cutaneous surface had

been involved. The extension was wavclike, with the advancing border of erythema always sharply margined. The skin posterior to the advancing border gradually became normal. Arcs of erythema would appear and disappear. There were constitutional symptoms, including arthritic manifestations, which are later discussed. The patient became partially incapacitated and depressed and took his life twenty-nine months after the onset of the infection. This generalization of the infection is rare in the literature of the disease.

Vesicles.—One or a few vesicles appeared on the skin at the site of erysip- eloid in seven cases. They were hemorrhagic and ap- peared as the first symptom in one case and soon dis- appeared. Few textbooks mentioned the occurrence of vesicles with erysip- eloid. Such vesicles were not men- tioned in Rosenbach's orig- inal description.

Lymphangitis and Adenitis.—These symptoms occurred in twenty-one cases. They appear early and disappear before the involved skin becomes nor- mal. In seven additional cases enlargement and tender- ness of the regional lymph nodes were noted in the absence of lymphangitis.

Constitutional and Arthritic Symptoms.—Six patients had a temperature ranging from 100 to 102 F. and had mild constitutional symptoms. One patient, infected



Fig. 4.—Erysipeloid of two days' duration in an abattoir employee following a puncture wound by a hog bone. The erythema was well defined and purplish red.

from a fish source, had chills, vomited and had pro- nounced lymphangitis and a temperature of 101.4 F. Another, infected from a swine source, had similar symptoms, with a temperature of 102 F., and was confined to bed for six days. Some patients stated that they felt ill and feverish the first few days of the infection.

Stiffness of the joints of the involved finger is a common symptom of erysipeloid. Such stiffness cannot be attributed entirely to the tenseness of the swollen finger, since it persists after the swelling disappears. At times there is an associated dull pain in the finger joints as well as the wrist (fig. 5), the elbow and even the shoulder.⁶ In ten cases in this series the arthritic symptoms persisted after the skin became normal. In five the joints of one or more fingers were involved and in four the wrist, elbow or shoulder, although in these cases the erysipeloid was confined to the hand. In a few cases puffiness around the involved joint was observed. The maximum duration of arthritic symptoms was eight months except in the case in which the infection became generalized. In this case arthritic symptoms were most conspicuous. During twenty-nine months of infection many joints became involved. The symptoms were dull ache, stiffness and loss of full motion, resulting in partial incapacitation. These symptoms were intermittent and were apparently at



Fig. 5.—Erysipeloid in a retail butcher who cut his wrist when handling pork. He had lymphangitis, adenitis and pain in his wrist. Immune serum (12 cc.) was injected locally, and there was a pronounced systemic reaction.

first periarticular, resulting from spread of the infection by continuity from the skin. Roentgenograms of the joints at first normal later showed changes.⁷

Relapse and Second Attack.—Relapse occurred in six cases, in four from two to five days after all evidence of the infection had disappeared and in two after two weeks. In two of these cases relapse occurred after local injection of 3.5 cc. and 10 cc., respectively, of immune serum. These figures do not include the case of generalized cutaneous involvement, in which there were many relapses. Only one patient in the series had a second attack, and this occurred at the site of injury four months after the first infection.

6. It is interesting to note the following statement in the report of G. B. Lawson and M. S. Stinnett (South. M. J. 26: 1068-1070 [Dec. 1933] of 247 cases of erysipeloid among workers in a bone factory: "Some of the patients complained of severe pain in the shoulder on the involved side." This was mentioned without reference to the arthritic phase in erysipeloid.

7. My experience is similar to that of S. Kartal (Die chronische menschlichen Schweinerotlauf, Deutsche Ztschr. 1935), who said that when the duration of erysipeloid was four weeks arthritic symptoms usually disappear with the cutaneous lesions and that when the duration is longer than four weeks such symptoms usually persist after disappearance of the cutaneous lesions. He described three forms of arthritic involvement associated with erysipeloid: (1) chronic recidive, arthritic symptoms persisting after cutaneous involution, (2) chronic stationary and (3) arthritis deformans. The third form is identified only from the history.

Treatment.—Rest and heat are important. The hand should be carried in a sling or, as is more preferable, in a splint. Wet or dry heat should be applied a few times daily. All variety of antiseptics and other agents, including foreign protein and roentgen therapy, have been recommended. Calloman⁸ favored a wet dressing of alcohol and also application of ichthammol. Mühlpfordt⁹ reported favorable results from intensive and repeated use of ultraviolet rays (Kronmayer lamp). Fränkel¹⁰ highly recommended local application of a 3 per cent alcoholic solution of acriflavine hydrochloride, followed by a dressing of ichthammol.

For local treatment I favor constant wet dressing of 12 per cent ichthammol in alcohol. Repeated erythema doses of ultraviolet rays with a water-cooled mercury quartz lamp (Kronmayer lamp) apparently are effective, according to my experience. I am uncertain as to the value of roentgen therapy. Patients to whom I gave such treatment did not do better than the control series. Indeed it is difficult to evaluate different methods of treatment, since in many cases erysipeloid apparently runs a self-limited course and splinting the hand may be the only required treatment. To judge by the course of the infection before and after local treatment, I believe that such treatment is effective. I discontinued the routine use of immune serum¹¹ injected either at the site of infection (fig. 5) or intramuscularly (fig. 3). Of forty-eight patients treated with serum, eighteen had serum sickness, and this frequently prolonged the period of incapacitation. I believe that serum is indicated if the infection persists one month, if it progresses rapidly, as in the case illustrated in fig. 3, or if arthritic symptoms are conspicuous. I then use large doses, from 100 to 150 cc. (provided cutaneous testing gives a negative reaction, like that shown in figure 3) injected intramuscularly in the course of a few days. Some of this amount I inject locally. A considerable variety of treatment (detailed elsewhere¹²), including the administration of a total of 450 cc. of serum, was ineffective in the case in which the infection became generalized.

Duration (from Onset to Recovery).—In ten cases the duration was from seven to ten days. Six of the patients were seen early and treated with local infiltration of immune serum (from 6 to 15 cc.), to which therapy the short duration was attributed. In the remaining four cases the infection was mild and was confined to the area originally involved. In another case also the infection was mild and did not spread; the duration was fifteen days. The five patients with a mild infection lost no time from their work, prompt improvement following local application.

The duration was one month in eight cases, forty-five days in one case, and two months, three months and eight months respectively in three cases. The maximum duration was twenty-nine months (at the time of death), in the case of generalized cutaneous involvement. In the remaining seventy-nine cases the duration ranged from ten to thirty days, and in the majority was about three weeks.

1934 Spruce Street.

8. Calloman, F.: Pseudoerysipel Erysipeloid, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1929, vol. 9, pt. 1.

9. Mühlpfordt, H.: Rotlaufserumbehandlung oder Höhensonnenintensivbestrahlung des Erysipeloids? Dermat. Ztschr. 60: 445 (April) 1931.

10. Fränkel, W. K.: Trypaflavinbehandlung des Erysipeloids, Dermat. Wehnschr. 51: 1967 (Dec. 19) 1931.

11. Immune serum was prepared by Dr. John Reichel of Sharp and Dohme, organism recovered from a patient infected from a fish source being employed. This serum in doses of 0.2 cc. protected white mice against 1,000 times the fatal dose.

ELECTROLYSIS CONTROLLING FACTOR
IN THE USE OF METALS IN
TREATING FRACTURES

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AND

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The use of metals in direct fixation of fractures is a very old procedure. There have been many disappointments and numerous investigations in the effort to find the reasons for the inconsistency of the end results. The factor of electrolysis in bone surgery was but vaguely suggested¹ until we undertook our experiments in 1936.² We undertook to ascertain whether electrolysis was demonstrable, what its effects were on bone and soft tissue, the clinical applications of this principle and finally, through clinical experience, the importance of electrolysis in the direct splinting of fractures with metals.

The initial reports of our experiments were presented before the Texas Surgical Society (October 1936) and the Southern Surgical Association (December 1936) and later published.² The results of further experiments, demonstrating the presence of electric current in vivo when contacts were made with metals in the bone and the early clinical applications of this phenomenon, were presented before the Southern Medical Association (December 1937) and the American Congress of Physical Therapy (September 1937).³ Thus we feel that a comparatively brief review of the further course of study and deductions, with final emphasis on the clinical import of electrolysis, may be sufficient.

CORROSION AND ITS CAUSE

In the search for metals for clinical use in the treatment of fractures, mechanical qualities alone have hitherto been stressed. More recently, however, efforts have been directed toward an attempt to avoid corrosion, since this has become recognized as the cause of changes in bone and tissue as well as of disintegration of the metals used. What is corrosion? It is the disintegration of a metal in its fluid environment. What causes corrosion? The answer is electrolysis. With perfect (100 per cent) freedom from moisture about a metal there is no corrosion, but with any moisture present electrolysis is initiated, as a result of which corrosion begins. To avoid corrosion, therefore, electrolysis must be eliminated, because electrolysis precedes corrosion.

How can electrolysis be prevented? One way is to keep the metal dry and protected from moisture. That is why steel bridges and metal roofs are painted. The other is to use a metal that is passive to its fluid environment or to find a metal that will be passive in certain fluids. Our interest of course is in some metal that will be passive (electrically neutral) in the human body fluids.

Read before the Section on Surgery, General and Abdominal, at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 15, 1938.

1. Galfre: Soc. de phys. et d'hist. nat. de Genève 47, 1930.
2. Venable, C. S.; Stuck, W. G., and Beach, Asa: The Effects on Bone of the Presence of Metals; Based upon Electrolysis, Tr. South. S. A. 49: 294, 1937; Ann. Surg. 105: 917 (June) 1937.
3. Venable, C. S.: Osteosynthesis in the Presence of Metals: Studies on Electrolysis, South. M. J. 31: 501, 1938; Electrolytic Action Between Metals as Used in Bone Surgery, Arch. Phys. Therapy 19: 285 (May) 1938.

ELECTRICAL NEUTRALITY VERSUS ELECTROLYSIS

What is meant by the passivity of a metal? The property of protecting itself from the effects of the surrounding moisture. This is accomplished by the instantaneous formation of a molecular veil about the metal as though it were sealed in cellophane. This fact, long a theory, has been proved by an Englishman, Evans, who has been able to remove this "molecular veil" and demonstrate its presence microscopically. Naturally the veil must be constantly present to be effective. If its molecules can be removed by agitation or movement the relative passivity of the metal is changed. This explains why in many instances bone plates and screws of various alloys have caused no disturbance in the body; they have become passified and remained so. Passivity will often result if there is no disturbance of the molecular veil of protection, if the fixation device in the bone is subject to no tissue motion over its surface, which may and does remove the protective veil, or if the metal becomes encysted so that the tissue movements do not affect or change the fluid with which it is in contact.

These phenomena can be effectively demonstrated by using sensitive instruments which will register the current established when a piece of zinc is immersed in

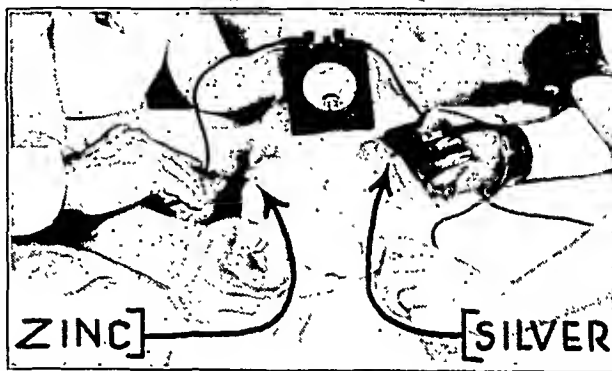


Fig. 1.—The current registered on a micro-ammeter between zinc and silver, contacts in the two femurs of the living animal.

salt solution at the anode and a piece of gold at the cathode. The registered current will soon cease if the gold electrode is kept perfectly still and will be started again if the gold is moved. Any motion of the metal causes the veil to be washed off, and the metal is no longer passive.

If, however, a metal that is inherently passive is substituted for the gold, it may be constantly agitated without producing a current, though the same contacts and solutions are used.

Relative to this work, lack of chemical knowledge and a desire to simplify the discussion have caused it to be stated that after all we are talking about oxidation. On the contrary, our critics have not understood the relationship between electrolysis and oxidation, and these statements have introduced needless confusion. Oxidation is the result of a chemical process involving the increase of positive charges on an atom or the loss of negative charges, and obviously this action must be preceded by electrolysis. Again, if no moisture is present there is no oxidation, just as there is no corrosion. Corrosion and oxidation are separate end results incident to electrolysis. These are electrical and chemical facts which cannot introduce difference of opinion or controversy.

To illustrate, a straight strip of platinum may be immersed in the electrolyte, both terminals then being cathodic, but if the platinum is bent the peak of the bend becomes anodic and current is established to the anode from each cathode. A more homely illustration is that of two galvanized iron nails, one bent, which are exposed equally to moisture. The straight nail will rust more slowly and uniformly because both ends are

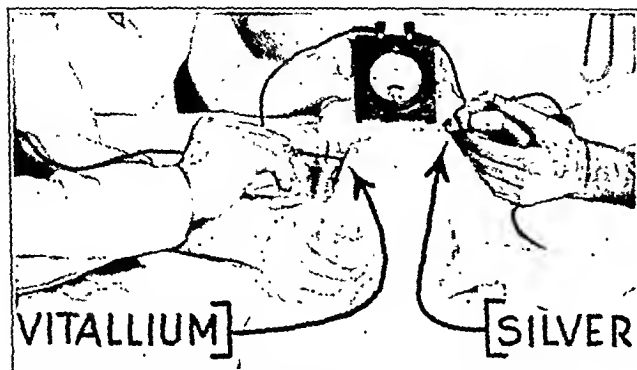


Fig. 2.—The absence of current between vitallium and silver, the poles being in opposite femurs of the living animal.

cathodic, while the bent nail will rust first on the convex peak of the bend. At that point, because of the molecular change of its atoms, an anode is created, and at once a current is established from each cathode to the anodic point, with resulting corrosion and oxidation. Finally, it is at the point at which the nail is bent that it will break. It is essential that these basic facts in chemical metallurgy be understood before passivity or electrical neutrality in a metal and the clinical application in the synthesis of bone with metals can be explained.

ELECTROLYSIS IN ALLOYS

In mixed metals or alloys there are great differences in electrical potential between the constituents, and the more metals that are used to create an alloy the greater this difference becomes. Moreover, it is easy to see that there is no way in which a single basic metal can be used commercially. A watch is from 14 to 18 carat gold; a dollar is only 48 per cent silver, and iron is melted and mixed with other metallic ingredients to make it hard or soft, rigid or ductile, as may be desired. In trying to create a strong alloy resistant to the body fluids, one must mix the metals so that there are no corrosive changes and no damage to the bone.

In our studies of electrolysis we deliberately set out to create batteries in the bones of living animals by using screws of mixed metals of different potentials which were not coupled. At autopsy biochemical examinations of the tissues about the screws revealed that ions of one metal had migrated to the neighborhood of another metal in accordance with the law of electromotive force of metals. This proved the presence of the effects of electrolysis. We then tried a number of the so-called rustless and noncorrosive steels in combination with baser metals and in each instance found changes in tissue, necrosis of bone and other electrolytic effects. We found, however, that there were no such effects when one alloy, vitallium, made of cobalt, chromium and molybdenum, was used. Our experiments were repeated several times to check and recheck the apparent fact that this singular alloy seemed consistently to remain inert.

CORROSION OF ALLOYS

In addition to performing animal experiments, we tried to demonstrate the presence or absence of corrosion about these different metals by mounting plates and screws made of them on glass and immersing them in physiologic solution of sodium chloride in sealed glass containers. The solutions in the jars quickly became muddy, and the plates showed the effects of corrosion within a few days. On the other hand, none of these phenomena were present when screws and plates of vitallium were used. The salt solution about the vitallium remained clear for months, with complete absence of corrosion or visual evidence of change in the solution. (Furthermore, we had a piece of vitallium hung off a dock in the Gulf to find out whether the constant wash of the sea would affect its passivity. After a month it was as bright as the day it was immersed.) Chemical examination of the solutions about the plates and screws of the metals other than vitallium revealed positive evidence of the metallic constituents of the metal. The solution about vitallium, however, showed no evidence of any metal from the plates or screws.

All these experiments were repeated by placing a single screw in physiologic solution of sodium chloride and in blood serum. The results were the same visually and by analysis, except in the case of the single screw of V2a or K2a ("Wipla metal"). This showed less visual change in the saline solution, but by analysis its constituent metals were recovered from the solution. The screw of vitallium caused no reaction in the fluids used, and qualitative chemical tests for metals were negative.

It is interesting to review what Haase, in collaboration with Magnus, has had to say⁴ concerning his experiments with rustless steel in the matter of corrosion based on electrochemical action. His work was published about a year and a half after our preliminary report. His observations entirely coincide with ours

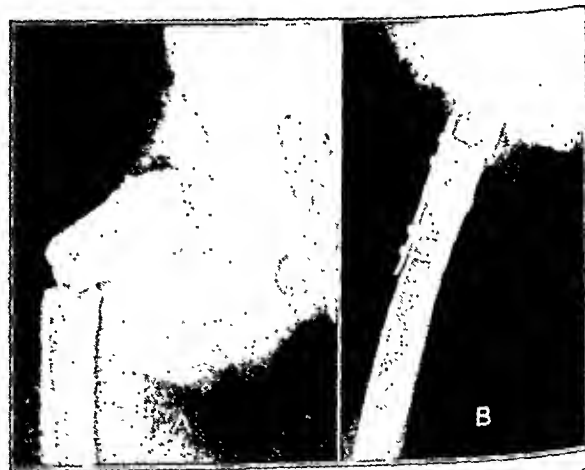


Fig. 3.—A, fracture through the site of an old cyst in the bone. B, union without disturbance of the bone; the engagement of the screws is tight four months after correction.

that V2a (18-8 rustless steel), though more resistant than most metals, does not remain passive or electrically neutral and shows evidence of electro-activity and corrosion in salt solution, sea water and body fluids.

With this proof of the presence of electrolysis about the metals commonly used in operations on bones

4. Haase, W., and others: Rustless Steel in Surgery, Arch. f. orthop. u. Unfall-chir.

and of the reactions in salt solution, blood serum and experimental animals, we undertook to demonstrate the amount of electric current involved by means of a micro-ammeter. A piece of silver wire was attached to the cathode and different metal Lane plates in turn to the anode, with physiologic solution of sodium chloride as the electrolyte. When any of the common metal appliances were used, more than 200 micro-amperes was registered. With vitallium, on the other hand, the micro-ammeter registered only two or three micro-amperes at the instant of immersion and immediately reverted to zero, where it remained in spite of agitation. When the poles were reversed and zinc was attached to the anode, with vitallium at the cathode, a slight momentary reversal of current was shown, which immediately disappeared. Even pure gold does not have this remarkable degree of passivity.

ELECTROLYSIS IN LIVING ANIMALS

Finally, to demonstrate the presence of an electric current between metal plates in the bones of a living animal, screws of different metals were placed in the tibia of a rabbit, and contact was made through a micro-ammeter while the body fluids acted as the electrolyte. In each instance except when a vitallium screw was

question the decalcification about the screws of electro-active (nonpassive) metals and the increased demineralization of bone at the site of plates and screws in old fractures. The changes are demonstrated by the recovery of an excess of calcium from the fluids collected about the area in which such metals have been used.

With the inherent characteristic of constant passivity of this strange alloy, vitallium, shown in all our experi-

Fifty-Seven Cases in Which Vitallium Was Used*

No. of Cases	Bone Involved	Period of Observation			End Result		
		3-6 Mo.	6-12 Mo.	Over 12 Mo.	Good	Fair	Poor
10	Femur.....	6	8	2	14	24	0
9	Tibia and fibula	6	3	0	7	11	18
3	Humerus.....	1	2	0	3	0	0
9	Radius and ulna	7	2	0	7	2	0
Total 37					31	3	1

† 1. Old compound fracture of the femur after four months had still not united. 2. Old compound fracture of the femur after seven months was still draining.

‡ One old compound fracture of the tibia after five months was still draining.

§ One old fracture of the tibia after four months had failed to unite because the plate was improperly applied.

Fresh Fractures (less than three weeks old)

No. of Cases	Bone Involved	Period of Observation			End Result		
		3-6 Mo.	6-12 Mo.	Over 12 Mo.	Good	Fair	Poor
9	Femur.....	8	1	0	8	14	0
4	Tibia and fibula	4	0	0	3	0	11
6	Humerus.....	4	2	0	6	0	0
1	Radius and ulna	1	0	0	1	0	0
Total 20					18	1	1

† Fracture of the hip three months after nailing was still quite stiff.

‡ Badly comminuted fracture of the tibia after five months was not united.

* In the entire series there was apparently no loosening or disturbance of the bone about any appliance except one screw. This was in the case of the compound fracture of the femur which was still draining.

used a strong current was registered. With vitallium there was a trace of current at the moment of contact, due doubtless to the thermal differences between the point of contact and the screw in the tibia.

We tried, furthermore, to determine whether the distance between the points of contact was of any moment. Holes were drilled in each femur of a rabbit and a silver screw placed in one and a zinc screw in the other. With this distance between the screws more than 200 micro-amperes was produced, while with screws of vitallium and zinc or vitallium and silver in the two femurs, only a momentary trace of current was seen.

When there is an electric current there is heat plus a disturbance in the electrolyte. This explains beyond



Fig. 4.—Interposition of vitallium cap over head of femur in correction of bony ankylosis. Patient ambulatory after eight weeks.

ments, with or without couple, in physiologic solution of sodium chloride, in blood serum and in vivo, we naturally turned to its application in human osteosynthesis. At this time we know of no other metal or alloy except vitallium which is so completely electrically neutral and sufficiently strong to meet our needs but we believe that, with the recognition of electrolysis as the controlling factor, metallurgists may develop others.

We began the use of plates, screws and nails made of vitallium about eighteen months ago, and in the past seven or eight months many surgeons in other parts of the country have undertaken their use. Their operations have been comparatively recent, and we include in our report only cases in which operation was performed three months or more ago, as we are more anxious to know what happens to the bone in the course of time after the insertion of an appliance made of this metal than we are simply to enumerate cases in which vitallium has been used in fixation.

In the accompanying table there are listed fifty-seven cases, including ours and those of five other surgeons, in which vitallium appliances were retained for three months or more. End results as to healing of the fracture were analyzed and the tolerance of this metal by healing bone was observed. It is our conclusion that there has been neither overstimulation of bone growth, with excessive callus, nor demineralization of bone at the fracture sites or about the screws or nails inserted in the bone.

Having proved the presence of electrolysis and its effects as between metals in operations on bone and the absence of pathologic changes in the bone when a metal which is electrically neutral and remains entirely passive *in vivo* is used, we believe that we may give as our opinion that the use of vitallium or any equally inert nonelectrolytic alloy in the fixation of old ununited or malunited fractures or even fresh fractures opens a new approach to this problem. Previously metals were banned in reconstructive operations on old fractures because they were believed to set up infection, to cause

pressure necrosis or in other ways to inhibit bone growth. We have proved that these complications were due to electrolytic destruction of bone about electrically active metals. On the other hand, when we have used vitallium plates, screws or nails in the repair of fractures we have found that perfect fixation has been obtained, there has been no necrosis of bone and the processes of bone repair have taken place promptly without preliminary decalcification. Thus we feel confident that this totally nonelectrolytic alloy will restore metal to a prominent place in all



Fig. 5.—The fixation of a fresh fracture of the patella by transfixion with a vitallium screw. The screw was applied without entering the knee joint.

phases of fracture work and reconstructive operations and will eliminate the need for such compromises as removable fixation or other temporarily applied devices.

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ABSTRACT OF DISCUSSION

DR. EDGAR L. GILCREEST, San Francisco: This study is epoch making. In the search for a metallic substance for the fixation of fractures a substance had to be secured that could be rendered aseptic and would not be irritating to the tissues. That was a difficult problem. In the solution there have been three stages. Surgeons all remember the stage of internal fixation by plates. Sir Arbuthnot Lane of London devised and popularized all kinds and shapes of beautiful plates, which became the rage in 1910; but most of these plates proved irritating, the wounds often became infected and tragedies often followed. In the second stage, or the period of fear, surgeons often did not know whether or not to operate. They felt that anything they did might prove wrong. In the third, or gadget stage, more and more external traction was used and innumerable inventive geniuses began to attach their names to their various gadgets to pull bones into place. The multiplicity of these mechanical devices is often confusing and frequently complicates the picture in the treatment of fractures. The surgeon should decide very early in the treatment of a fracture whether he will use an open or a closed method, and if he decides on a closed method he has a reliable friend in vitallium, which

the authors' experimental and clinical experience has proved is an ideal metallic substance, tolerated by the healing bone and surrounding tissues.

DR. LEON O. PARKER, San Francisco: From clinical, microscopic and chemical studies of the steel alloys implanted in tissues, it appears with reasonable certainty that none of them are tolerated or can be trusted to be tolerated permanently. I wish to warn clinicians who are using stainless steel wires or other stainless steel instruments that cannot be removed. When a very small caliber wire is used and a number of loops or coils are encircled about the fractured ends of the bone for fixation, union is frequently shown in the early stages of the fracture and there may be very little disturbance of the tissue for a few months although sclerosis and ebonation in the region of the wire appear later and are followed by pathologic fracture due to the metallic substances. Most surgeons have felt that the tissue intolerance of metal was simply a question of toxic metallic ions being given off from the surface of the metal and redeposited in the tissues in the form of oxide, if it was an iron atom; in the case of chromium, which is more soluble, there is no redepositing in the area of implantation. However, with the work of Drs. Venable and Stuck one must come to the conclusion that it is not necessarily a toxic metallic ion but a toxic metallic electron, the electrochemical phenomenon of electrolysis being in direct proportion to the tissue intolerance. Whether the role of pathogenesis is assigned to this electrochemical phenomenon, which of course cannot be separated from the simple chemical nature of the metal, or to the simple chemical nature of the metal does not matter. These studies show that vitallium is a passive metal, electrochemically, when buried in the tissues, and the chapters on implantation of metals for the fixation of fractures and other uses must be rewritten. With this start the use of the proper metals for the replacement of destroyed segments of bone or joints deserves serious consideration for both further research and clinical trial.

DR. C. S. VENABLE, San Antonio, Texas: The question now is not the fear of pressure necrosis or the tissue changes and discolored fluid erroneously thought of as infection. It is now known that such changes are due to electrolysis. One can now understand why metals in the synthesis of bone, used with such variable success, have gone largely out of vogue in favor of autogenous bone grafts, particularly for older fractures which are already atrophic and demineralized. The use of these mechanical appliances, which suffice to hold the fragments, has on too many occasions resulted in loosening screws, broken appliances and nonunion. The screws could be picked out with the fingers, and a terminal result of fibrous union occurred too frequently as a result of progressive demineralization, a factor secondary to electrolysis; metal plates crossing a fracture site fixed by screws, all the appliances of metals of different potentials, brought about these conditions, and the resulting nonunion had nothing to do with pressure necrosis, as heretofore believed. We are sorry that the appliances made of the metals which we have previously used, particularly rustless steel, have not proved to be electrically neutral and so usable for fracture work, because they may be milled so that any appliance can be made and at less cost; but so long as they do not stand up, it is only proper to report our experience in checking these experiments. This cobalt-chromium alloy, which is electrically neutral and causes no disturbance of the tissue, is too hard to be milled and is limited in application because each article has to be separately cast. We feel that the criterion in the matter of osteosynthesis with metals is that the metal must be electrically neutral or entirely passive in the presence of the body fluids and sufficiently rigid and strong to do its part mechanically. Surgeons are fortunate in having this metal, which we have found to be entirely resistant to body fluids, or passive. Metallurgists may develop other alloys which will meet these conditions; the criterion must be that the metal is passive and retains its molecular veil of passivity in the presence of agitation or friction and remains passive *in vivo*. With this principle carried out, we believe that an era of osteosynthesis with metals may be approached with greater confidence in the end results.

THE TREATMENT OF ACUTE INFECTIONS OF THE CENTRAL NERVOUS SYSTEM WITH SULFANILAMIDE

JOSEPHINE B. NEAL, M.D.

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Acute infections of the central nervous system may be roughly divided into those due to viruses and those due to bacteria. Table 1 gives a list of the diseases that are certainly or probably due to viruses. To this list might be added the Guillain-Barré syndrome, which is believed by some authorities to be due to a virus and by others to be due to avitaminosis.

There has been no experimental work giving favorable results with sulfanilamide in the treatment of any of these diseases except choriomeningitis.¹ With this disease it will be difficult to prove such results clinically, as patients presenting the symptoms of lymphocytic choriomeningitis usually recover before the diagnosis is established by laboratory work.

However, there is some hope that a compound of sulfanilamide may be elaborated that will affect the human virus diseases, since Dochez and Slanetz² have shown that a derivative of sulfanilamide is very effective in the treatment of distemper, a virus disease, in dogs and cats. Their work has been corroborated by Marcus and Necheles.³

Although many highly scientific papers have been written on the various compounds of sulfanilamide, it may be well to speak briefly of the relationship between prontosil (the disodium salt of 4-sulfamidophenyl-2'-azo-7'-acetylamino-1-hydroxynaphthalene-3',6'-disulfonic acid) and sulfanilamide.

The chemical referred to in this paper as prontosil (the name of which is to be changed to neoprontosil) is not the same as the earlier, less soluble preparation synthesized by Mietzsch and Klarer.⁴ My associates and I agree with Brown and Bannick⁵ of the Mayo Clinic that the relation of prontosil to sulfanilamide is peculiar and not clearly understood at the present time. As prontosil yields only 11 grains (0.73 Gm.) of sulfanilamide per hundred cubic centimeters of a 2.5 per cent solution, it is difficult to believe that the satisfactory results observed after the administration of from 40 to 100 cc. daily can be attributed solely to the sulfanilamide fraction of prontosil. It would seem that prontosil is capable of producing some other chemotherapeutic action in the body. Recently Barlow⁶ reported that the oral lethal dose of prontosil for laboratory animals was nearly seven times as great as that of sulfanilamide.

Other workers report favorably on the antistreptococcic effect of prontosil administered orally. With these statements our experience inclines us to agree.

From the Bureau of Laboratories, Department of Health, New York City.

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1. Rosenthal, S. M.; Wooley, J. G., and Bauer, Hugo: Pub. Health Rep. 52:1211 (Sept. 3) 1937.

2. Dochez, A. R., and Slanetz, C. A.: Science 84:142 (Feb. 11) 1938.

3. Marcus, P. M., and Necheles, Heinrich: Proc. Soc. Exper. Biol. & Med. 35:385 (April) 1938.

4. Domagk, Gerhard: Deutsche med. Wchnschr. 61:250 (Feb. 15) 1935.

5. Brown, A. E., and Bannick, E. G.: Proc. Staff Meet., Mayo Clin. 12:644 (Oct. 13) 1937.

6. Barlow, O. W.: Proc. Soc. Exper. Biol. & Med. 37:315 (Nov.) 1937.

While we have not used prontosil orally as much as sulfanilamide and prontosil by injection, we have had rapid and remarkable improvement following the use of prontosil by mouth.

In spite of all the work that has been done with sulfanilamide, prontosil and various other compounds, there is still considerable difference of opinion with regard to the proper dosage, the best compounds and the best route of administration.

We have always used a much smaller dose than has been recommended by certain authorities. Indeed, recent experimental work by Osgood⁷ would seem to indicate that small doses at frequent intervals are more effective than larger doses at longer intervals. As a rule we have given 5 cc. or less of the prontosil solution every four hours to young children and 10 cc. every four hours to older children and adults. In addition from 5 to 15 grains (0.32 to 1 Gm.) of sulfanilamide has been given every four to six hours. The same dosage was followed when prontosil was given by mouth. At present we are inclined to use prontosil orally unless the patient cannot swallow or

TABLE 1.—Virus Diseases of the Central Nervous System

	Disease	Etiologic Agent
A. Definitely known that virus is cause	1. Human rabies	Virus of rabies
	2. Poliomyelitis	Virus of poliomyelitis
	3. Louping ill	Virus of louping ill
	4. St. Louis type of encephalitis	Virus pathogenic for mice and less so for Macacus rhesus monkeys
	5. Lymphocytic choriomeningitis	Armstrong's or Traub's virus
	6. Japanese type B encephalitis	Virus pathogenic for mice and Macacus rhesus monkeys
B. Highly probable that virus is cause	1. Epidemic encephalitis	Neurotropic herpetic-like virus?
	2. Australian X-disease	Virus pathogenic for rabbits, monkeys, sheep and colts
	3. Encephalitis secondary to measles, varicella, whooping cough and other acute infections	?
	4. Encephalitis secondary to vaccination	?
	5. Meningo-encephalitis following mumps	Probably virus of mumps

retain medication given by mouth, under which conditions it is given by injection. We occasionally administer prontosil intraspinally, using an equal amount of prontosil (2.5 per cent) and a specific serum, if available, or sterile physiologic solution of sodium chloride or sterile distilled water. It should be pointed out that the p_H of prontosil is now 6.8, which is compatible with its intraspinal use.

While sulfanilamide is a therapeutic agent of great value, it has toxic effects of more or less importance. The most serious are those associated with the hematopoietic system; namely, hemolytic anemia and agranulocytosis. The development of morbilliform rashes and fever are less serious. Mild toxic effects are quite common, and they include cyanosis, dyspnea, dizziness, nausea, headache, excitement and confusion. Certain of these reactions appear to be direct toxic effects of the drug, while others, particularly hemolytic anemia and agranulocytosis, must be regarded at present as idiosyncrasies. Fortunately, we have not encountered any of the more serious reactions.

With the development of the more severe toxic manifestations the drug should be withdrawn at once. We

7. Osgood, E. E.: Culture of Human Marrow: Studies on Mode of Action of Sulfanilamide, J. A. M. A. 110:349 (Jan. 28) 1938.

do not, however, consider cyanosis as an indication to discontinue the administration of sulfanilamide. It should be noted that the oxygen-carrying capacity of the red blood cells is not diminished during the period of cyanosis. Dyspnea, which is due to acidosis, can usually be prevented by the routine administration of sodium bicarbonate in conjunction with the sulfanilamide. When the alkali cannot be given by mouth, one may administer a one-sixth molar solution of sodium lactate by the intravenous or subcutaneous route.

It is important in administering sulfanilamide to make frequent, complete blood counts.

Sulfanilamide has its greatest value in the treatment of diseases of the central nervous system due to bacteria. These are, of course, primarily meningitis and infections of the accessory sinuses and mastoids which may lead to meningitis and to brain abscesses. Our experience has been greatest in the field of meningitis. Table 2 shows the distribution by age and

TABLE 2.—Cases of Meningitis According to Age of Patient and Etiologic Agent*

Age	Meningococcus	Streptococcus	Pneumococcus	Bacillus Influenzae	Bacillus Tuberculosis	Miscellaneous Organisms	Total
1, 2, 3 mo.....	47	14	10	3	4	14	92
4, 5, 6 mo.....	87	10	6	15	27	10	155
7 through 12 mo.....	97	4	17	23	107	21	271
Total under 1 year.....	231	28	33	43	138	45	518
1-2 years.....	100	6	14	40	192	10	362
2-3 years.....	65	13	12	20	114	10	234
3-5 years.....	164	24	20	27	167	12	414
5-10 years.....	269	107	35	16	143	30	600
10-20 years.....	324	37	33	8	110	43	555
Over 20 years.....	401	54	102	10	133	78	778
Age not stated.....	12	5	6	0	13	5	41
Total.....	1,566	274	255	164	1,010	233	3,502

* During 1937, 147 additional cases of meningitis were observed.

etiological agent of our cases of meningitis over a long period of years. Since this table was prepared we have observed about 200 additional cases of meningitis.

With regard to infections with the meningococcus, I am of the opinion that serum should be used intraspinally in conjunction with some form of sulfanilamide, preferably prontosil, given either orally or hypodermically. Experimentally it has been shown that a combination of serum and sulfanilamide is more effective than either agent alone.⁸ I realize that Schwentker⁹ and others have reported favorable results in the treatment of meningococcal meningitis with sulfanilamide only. From a somewhat limited experience I do think that sulfanilamide may replace the use of serum in the treatment of meningococcemia.

During the past five or six years there has been a decided increase in meningitis due to *Bacillus influenzae*. Povitzky¹⁰ found experimentally that mice were effectively protected against lethal doses of the strain *B. influenzae* commonly associated with meningitis by the use of prontosil and a specific serum.

With this form of meningitis the clinical results have not corresponded with the experimental results. In treating this form we have used the specific serum intraspinally and also, as bacteremia is often present, intravenously. Recently we have been combining the serum with prontosil for intraspinal use. Sulfanilamide is given also, by other routes. The results, however, have been disappointing. Of eighteen patients only two have recovered.

It has been reported that sulfanilamide combined with serum was as efficacious experimentally with certain strains of pneumococcal infections as with hemolytic streptococcus infections. Our clinical results have not corroborated this observation in the case of pneumococcal meningitis.

Pneumococcal meningitis was uniformly fatal in our experience of nearly twenty-seven years until we began the use of sulfanilamide. Since that time we have had thirty-three cases with six recoveries and one under observation. The recoveries were from types XXXI, XXIX, IV, XIII, VI and VII. The patient with type VI received rabbit serum also. The patient with type VII received horse serum. It should be pointed out that in several of the fatal cases the course was prolonged, with periods of improvement. When a specific serum is available it is combined with prontosil and injected intraspinally. It has seemed to us that one reason at least for the relative lack of success of sulfanilamide in the treatment of pneumococcal meningitis is that foci of infection have been so seldom located and removed. We have seen the recovery of two patients with meningitis for whom the hospital reported the type II pneumococcus.

We have also observed a certain group of cases that may be classed as miscellaneous. Some of the patients had a brain abscess and meningitis, the latter being due in one case to a hemolytic streptococcus, in another to *Staphylococcus aureus* and in a third to a mixed infection. In a fourth case there was a brain abscess due to *B. influenzae* without meningitis. The patients all died. In a fifth case of brain abscess following otitis media and mastoiditis, in which *Streptococcus hemolyticus* was isolated, recovery took place. The patient had received sulfanilamide during the acute phase of the otitis media and also before and following the operation on the mastoid and the abscess. She made a complete recovery without the development of meningitis.

The use of sulfanilamide in cases of hemolytic streptococcus meningitis has yielded the most revolutionary results. Before this chemical was used the case fatality was more than 95 per cent. Since its use the rate has been less than 20 per cent in a group of twenty-seven cases. Table 3 shows the outstanding features of these cases with the exception of the twenty-seventh, which is still under observation. The diagnosis was definitely established by recovery of the hemolytic streptococcus from the spinal fluid by culture. In this connection it is important to stress that certain strains of this organism hemolyze only horse blood and in mediums which do not contain sugar. Unless this is borne in mind, the hemolytic streptococcus will occasionally be misinterpreted as belonging to the non-hemolytic group.

It will be noted that sulfanilamide was used less than twelve hours in two, and less than twenty-four hours in one, of the five fatal cases. In the fourth fatal case the necropsy showed herniation of the cerebellum

8. Branham, S. E., and Rosenthal, S. M.: *Pub. Health Rep.* 52: 685 (May 28) 1937.

9. Schwentker, F. F.: *M. Clin. North America* 21: 1449 (Sept.) 1937.

10. Povitzky, O. R.: *New York State J. Med.* 37: 1748 (Oct.) 1937.

through the mastoid wound and thrombosis of the left lateral and transverse sinuses and of the left jugular vein.

These results seem little less than astounding to us who have been working so long and so unsuccessfully

In addition I should like to refer to two cases of meningitis following otitis and mastoiditis, in which the spinal fluid was that of meningitis, with gram-positive diplococci on smear but negative cultures. Both the patients recovered.

TABLE 3.—Cases of Meningitis Due to the Hemolytic *Streptococcus*

Case	Sex	Age, Years	Primary Source of Infection	Treatment	Result	Comment
1	♀	21	Maxillary sinusitis on right, otitis on right with mastoiditis	Drainage of antrum, mastoidectomy, spinal drainage, sulfanilamide, convalescent scarlet fever serum	Recovered	Only a small amount of serum was given
2	♀	7	Otitis on left with mastoiditis	Mastoidectomy, spinal drainage, sulfanilamide	Recovered	
3	♂	5½	Otitis on left	Antimeningococcus serum (4 doses), spinal drainage, sulfanilamide	Recovered	
4	♀	43	Otitis on right	Spinal drainage, sulfanilamide	Recovered	
5	♀	3½	Otitis on left	Spinal drainage, sulfanilamide	Recovered	
6	♀	11	Otitis on right with mastoiditis	Spinal drainage, sulfanilamide	Recovered	Refused operation and mastoiditis persisted after recovery from meningitis
7	♀	2	Double otitis with mastoiditis on right, following scarlet fever	Mastoidectomy on right with ligation of right jugular vein, spinal drainage, sulfanilamide, convalescent scarlet fever serum	Died	Meningitis appeared 7 days after operation; necropsy showed herniation of cerebellum and thrombosis of left lateral and transverse sinuses and of left jugular vein
8	♂	5½	Otitis on left with mastoiditis, following pneumonia	Mastoidectomy, antimeningococcus serum, spinal drainage, sulfanilamide	Recovered	
9	♂	8	Otitis on right with mastoiditis	Mastoidectomy 1 month prior to meningitis, spinal drainage, sulfanilamide	Recovered	Mastoidectomy done about 1 month before onset of meningitis; spinal fluid showed positive culture for 14 successive days
10	♀	4	Otitis on left with mastoiditis, and later otitis on right	Mastoidectomy on left, spinal drainage, sulfanilamide	Recovered	At operation left mastoid found necrotic, although no clinical signs
11	♂	35	Pansinusitis	Antimeningococcus serum, spinal drainage, sulfanilamide	Died	Sulfanilamide was used for less than 24 hours; necropsy showed pansinusitis and sarcoma of pituitary
12	♀	12	Otitis on left with mastoiditis	Mastoidectomy, spinal drainage, sulfanilamide, 1 dose antimeningococcus serum	Recovered	At operation mastoid found necrotic, although no clinical signs
13	♀	10 mo.	Double otitis with double mastoiditis	Mastoidectomy, spinal drainage, sulfanilamide	Died	Clinical evidence of brain abscess; at operation, dural plate found nearly destroyed; sulfanilamide used for less than 12 hours
14	♀	8	Otitis on left with mastoiditis	Mastoidectomy, spinal drainage, convalescent scarlet fever serum, sulfanilamide	Recovered	At operation mastoid found necrotic, although no clinical signs
15	♀	6½	Otitis on right with mastoiditis	Mastoidectomy, spinal drainage, sulfanilamide	Died	Necropsy showed meningitis but no localized suppuration
16	♂	4	Following measles, otitis with mastoiditis first on left and later on right	Mastoidectomy first on left and later on right, spinal drainage, sulfanilamide	Recovered	Meningitis appeared 12 days after mastoidectomy on left; at this time a mastoidectomy on right was done
17	♂	7	Double otitis with double mastoiditis following scarlet fever	Mastoidectomy first on left and 3 weeks later on right, spinal drainage, sulfanilamide	Recovered	Onset of meningitis was about 12 days after the second mastoidectomy
18	♀	11 mo.	Infection of upper respiratory tract	One spinal drainage, antimeningococcus serum, sulfanilamide	Died	Death in less than 12 hours after receiving sulfanilamide
19	♀	6	Double otitis, double mastoiditis	Double mastoidectomy, spinal drainage, sulfanilamide	Recovered	
20	♀	8	Chronic otitis on left	Spinal drainage, sulfanilamide orally, prontosil intramuscularly and intraspinally, mastoidectomy	Recovered	Mastoid at operation showed granulation, but no pus; blood culture sterile
21	♂	2	Otitis on right	Spinal drainage, sulfanilamide	Recovered	No signs of mastoiditis
22	♂	15	Bilateral chronic otitis	Spinal drainage, sulfanilamide, mastoidectomy on left and 2 months later on right	Recovered	Meningitis cleared up shortly after first operation
23	♂	7	Otitis on right and mastoiditis	Spinal drainage, sulfanilamide, mastoidectomy	Recovered	
24	♀	12	Otitis on right	Spinal drainage, sulfanilamide orally and intravenously	Recovered	
25	♀	11	Otitis on right	Spinal drainage, prontosil intramuscularly and intraspinally, prontosil orally	Recovered	
26	♀	7	Throat infection	Spinal drainage, prontosil intramuscularly, sulfanilamide orally	Recovered	Röntgenogram of sinuses and mastoid negative

with this form of meningitis. The question is sometimes raised as to the possibility that the hemolytic streptococcus may recently have become more benign. Such a radical and sudden change seems to us improbable. During the year 1936 we saw twenty patients with this type of meningitis, all of whom died with the exception of one who had had scarlet fever and who was treated with small amounts of sulfanilamide and large amounts of convalescent serum.

I consider sulfanilamide and its various compounds, especially prontosil and prontosil soluble, one of the major achievements in chemotherapy. It has been used too short a time for one to feel certain of the best dose and mode of administration. The full scope of its use in various bacterial infections is not yet known. Indeed, in spite of all that has been done, the drug is still in its infancy. One cannot look forward into the future to see what new developments

may take place in the next few years or even months. The intensive research work which is being carried on makes it quite certain that there are new and important developments yet to come.

ABSTRACT OF DISCUSSION

DR. R. CANNON ELEY, Boston: At the Infants' and Children's hospitals of Boston we have been interested in this new agent and have had the opportunity to administer it in certain infections of the central nervous system. The results have been in accord with those which have just been reported. Dr. Neal has roughly divided these infections into two groups, namely those due to virus invasion and those due to invasion by bacteria. I shall confine my remarks to the value of the drug in certain of the bacterial infections of the central nervous system. During the ten year period prior to the use of sulfanilamide, 118 patients with meningococcal meningitis received antimeningococcus serum therapy with a mortality rate of 39 per cent. Since the introduction of the dye, thirteen patients have been treated by this drug alone with only two deaths. The two patients that died were both suffering from a type II meningococcus infection. During the same ten year period, ninety-two patients with hemolytic streptococcus meningitis were treated by the usual methods and of this group there was only one recovery. These results are in sharp contrast with those obtained since the introduction of sulfanilamide, for we have now treated six patients with six recoveries. Seventy-three patients with pneumococcal meningitis have been admitted to the hospital, and of this group forty-three received specific serum therapy and only one recovered; this patient had a type XII infection. Six patients with pneumococcal meningitis were treated with the usual dose of sulfanilamide, and all died. That larger doses than we have used may bring about a reduction in the mortality rate has been suggested by the work of Finland, at the Boston City Hospital, who has reported ten cases of pneumococcal meningitis treated by the combined use of specific serum and sulfanilamide, with six recoveries. In each of these cases the dosage employed was sufficient to produce a concentration of from 25 to 35 mg. per hundred cubic centimeters in the cerebrospinal fluid. Ninety-six patients with influenzal meningitis have been treated with specific serum and of this group there were six recoveries; six additional patients have received combined serum and sulfanilamide treatment with no recoveries; one other patient received sulfanilamide in amounts sufficient to produce a concentration of 25 mg. per hundred cubic centimeters in the cerebrospinal fluid and recovered. The fact that this patient recovered has suggested that better results might be obtained if larger amounts of the drug were employed in the treatment of this form of meningitis. The methods which we have employed in the administration of sulfanilamide in meningitis have varied as our knowledge of the drug has advanced. When first introduced as a therapeutic agent it was given intrathecally as well as by mouth and by hypodermoclysis, as the case indicated, but since it has been shown that following oral administration the concentration of sulfanilamide in the cerebrospinal fluid is nearly equal to that in the blood stream, intraspinal treatment has been discontinued. In those instances in which the drug cannot be given orally we have resorted to the subcutaneous or intravenous injection of an 0.8 per cent solution of the basic salt in physiologic solution of sodium chloride.

DR. H. W. WOLTMAN, Rochester, Minn.: I shall confine my remarks to meningitis and closely related disorders caused by the streptococcus. Before the application of sulfanilamide in treatment, the mortality rate from streptococcal meningitis was 95 per cent. The treatment involved the most energetic measures that physicians could devise and patients could endure. Indeed, it so happened in our cases that those patients recovered who had had the simplest method of treatment, namely repeated spinal punctures. We had often heard of good results that were attributed to this or that method of treatment, but when such reports concerned larger series of cases there was usually lacking a demonstration of the causative organism. I need not say that the lack of such bacteriologic studies represents a crucial omission. Against the background of a mortality rate of 95 per

cent, Dr. Neal places the new figure of 20 per cent, a result achieved largely by the intelligent use of sulfanilamide. I need hardly mention such technical advances in the treatment as the insertion of a urethral catheter for purposes of controlled drainage and medication, as described by Dr. Love. This I have found very helpful. As with any new method of chemotherapy, the introduction of related drugs and the details of their administration remain to be worked out as our experience with them grows. Dr. Neal previously stressed another point in treatment, namely the attention that foci of infection, particularly in the mastoid process, deserve. Since she made this suggestion my associates and I have not hesitated to employ any additional surgical measures that seemed advisable even when patients were critically ill. Our experience parallels hers, and we stand ready to endorse her contention in this respect. The association of brain abscess with meningitis raises some interesting points. We have seen abscesses develop after streptococcal meningitis apparently had been brought under control. In one case rupture of the abscess into the ventricle occurred, but operation and the continued administration of sulfanilamide led to recovery. Sulfanilamide can hardly be expected to be helpful when diseased regions are out of its reach. This occurs when extensive thrombosis and infection are associated, but it is conceivable that with additional surgical treatment better results may be achieved even here. Dr. Neal speaks on the basis of an almost unparalleled experience. She has supplied us with a reliable background of things as they were and has helped to orient us with regard to things as they are developing.

DR. JOSEPHINE B. NEAL, New York: I am grateful for the suggestion that very large doses of sulfanilamide may be more effective in pneumococcal and influenzal meningitis than the smaller doses that I have been using. I shall try that in the future and hope to parallel the results which Dr. Eley has described.

HEPATITIS

SOME FORMS NOT COMMONLY RECOGNIZED

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A physician who has many contacts with the medical and surgical aspects of biliary and hepatic disease soon encounters surprises and embarrassments occasioned by the fact that hepatic disease, either as a complicating factor in extrahepatic biliary obstruction or as an independent entity, often comes on unawares. Thus, while in the majority of cases sufficient symptoms and signs are present to permit a diagnosis of obstruction of the common duct or of primary hepatic disease, there is a certain number of cases wherein the two conditions cannot be distinguished readily and the fundamental disease is misinterpreted. Moreover, in certain cases of primary hepatic disease the syndromes present are those commonly encountered in association with surgically relievable obstruction of the common duct. Furthermore, in cases of cholecystitis with stones and obstruction of the common duct (most frequently due to calculus) there may be associated hepatic disease which may readily be overlooked and which may have a significant part in the course of the patient's illness either before or after surgical procedures. In chronic cases this associated disease may be extensive chronic atrophy of the liver, and in cases of acute obstruction of the common duct the associated disease may be varying degrees of acute hepatic degeneration. These conditions often do not receive sufficient emphasis.

In the absence of jaundice, the occurrence of ascites, pruritus, enlargement of the liver or spleen, hematemesis

From the Division of Medicine, the Mayo Clinic.
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or melanoderma may indicate the presence of hepatic disease. However, there are many hepatic conditions in which these symptoms or signs are absent and in these instances diagnosis must rest largely on suspicion. In a considerable group of systemic diseases, such as the infectious processes, toxemias and neoplastic and leukemic infiltrations, it is generally recognized that the liver may be involved, yet in many instances the hepatic involvement is not suspected and in most instances the full extent of the damage is not appreciated at the time of the illness because of the lack of any of the usual symptoms of hepatic disease. In addition, there are other cases of hepatic disease without jaundice, unassociated with other systemic disease, wherein the possibility of hepatic involvement is not considered and the true nature of the disorder is not recognized.

Recognition of these facts, a healthy suspicion of the possibilities of such conditions as have been mentioned, and the judicious use of hepatic functional tests will aid greatly in demonstrating hepatic disease that is unsuspected or asymptomatic but which, nevertheless, is of considerable significance. When the presence of hepatic disease has been demonstrated, the functional tests aid materially in evaluating the degree of damage and in indicating the prognosis. This perhaps applies particularly to those conditions wherein surgical procedures are contemplated.

In this discussion the term "hepatitis" is used in a noncommittal manner to denote diffuse processes involving the liver and it may include such changes as cloudy swelling, fatty or other types of degeneration, atrophy and necrosis of varying type or degree. Fibrosis and even nodular regeneration may or may not be associated. The material is presented under the following titles, and short reports of cases are used to illustrate some of the forms of hepatitis not commonly recognized: (1) hepatitis associated with diseases of the gallbladder and biliary tract, (2) hepatitis associated with syphilis and its treatment, and (3) hepatitis without jaundice.

HEPATITIS ASSOCIATED WITH DISEASES OF THE GALLBLADDER AND BILIARY TRACT

Primary hepatic disease may mimic perfectly certain disorders of the extrahepatic bile passages, notably those caused by stones. Conversely, the secondary hepatic damage caused by stone and infection may be completely masked by the features of mechanical obstruction to flow of bile.

CASE 1.—A man aged 46, a moderate partaker of alcohol, had suffered for fifteen years from gaseous dyspepsia and attacks of pain of varying severity and increasing frequency in the right upper abdominal quadrant. These attacks were at times associated with chills and fever. A severe attack led to the patient's hospitalization. For twenty years dyspnea without orthopnea had been progressively developing. Edema of the ankles had been present for two weeks. On examination severe pain was evident. The temperature was 104 F. The right upper quadrant of the abdomen was moderately rigid and tender. Moderate jaundice was first noted on the day of admission. Laboratory investigations revealed a leukocyte count of 27,400 per cubic millimeter of blood, marked macrocytosis, bilirubin of 6.2 mg. per hundred cubic centimeters of serum, a direct van den Bergh reaction, cholesterol of 214 mg. and cholesterol esters of 103 mg. per hundred cubic centimeters of plasma, and serum proteins of 5.5 Gm. per hundred cubic centimeters. The albumin-globulin ratio was 1/1.6, and the excretion of hippuric acid was 0.37 Gm. At exploration a small hobnail liver and slight ascites were found.

This patient presented the syndrome commonly attributed to the presence of stone in the common duct.

namely recurring colic, chills, fever, jaundice and leukocytosis. Exploration was carried out on the basis of this diagnosis although it did not explain the dyspnea and edema. There were no cardiac, renal or pulmonary pathologic changes to account for these symptoms. The slightly lowered concentration of serum protein, the reversal of the albumin-globulin ratio and the decreased excretion of hippuric acid indicated hepatic disease. Although primary hepatitis masquerading as a calculus of the common duct is not a frequent occurrence, in our experience at the Mayo Clinic it has been noted sufficiently often that we feel somewhat more emphasis should be placed on such a possibility and on the results of hepatic functional tests.

A similar situation exists in cases in which jaundice is present and calculous cholecystitis has been demonstrated definitely by roentgenologic or other methods. In these instances the possibility of calculi being present in the common duct is considerably enhanced. Mild and transitory disturbances of the liver, as determined by functional tests, are not uncommonly encountered after acute cholecystitis or even biliary colic and are well recognized. The evidence is obtained chiefly by the rate of excretion of bromsulphalein or similar dyes and the character of the van den Bergh reaction. Clinically, the disturbance may be manifested by mild, transient jaundice. More advanced stages of hepatitis are also encountered and should be more frequently suspected, especially in the presence of long-standing cholecystitis or, if there is an enlarged liver, considerable decline in general health and jaundice of short duration. Enlargement of the liver often is accompanied by some splenomegaly. Other clinical symptoms previously mentioned may be present and increase the evidence of significant hepatic disease. In many of these cases the liver may appear to be in surprisingly good condition at operation whereas in others it is markedly cirrhotic and the post-operative course unsatisfactory. Whether or not surgical operation should be undertaken in these cases is frequently a difficult decision to make. Factors which influence this decision are the general condition of the patient, the degree of trouble the gallstones are producing and the evaluation of reserve capacity of the liver by the use of the various hepatic functional tests. Abnormalities elicited by these tests caution the physician concerning increased operative risk, necessity for prolonged preoperative preparation and the possibility of an unfavorable prognosis.

Two complications that may arise in the course of calculous obstruction of the common duct are acute degenerative conditions and chronic hepatitis. The following case is an example of the former:

CASE 2.—A man aged 43 had suffered from biliary colic during the preceding three years. The last attack had occurred ten days before his admission and was followed by persisting jaundice. Deep jaundice and slight tenderness in the right upper quadrant of the abdomen were evident on examination. Laboratory examinations disclosed small amounts of bile entering the intestine, a concentration of serum bilirubin of 19.7 mg. per hundred cubic centimeters, a direct van den Bergh reaction, normal galactose tolerance and a value for blood cholesterol of 340 mg. per hundred cubic centimeters. At operation a thick walled and distended gallbladder, containing pus and "white bile," without stones, was found. The common bile duct was dilated and from its lower end a stone 1.2 cm. in diameter was removed. A T tube was placed in the common duct for drainage. Hepatitis, grade 4, was present. The liver was described as brownish purple and the lobules stood out as punctate areas. Postoperatively, bile drained in rather large amounts (from 750 to 1,000 cc. daily). On the fifth day the

patient became rather drowsy but improved following intravenous administration of dextrose solution. There was a slight rise in the concentration of serum bilirubin, followed by a gradual fall to 4.3 mg. per hundred cubic centimeters on the fifteenth day. Six months later excretion of bromsulphalein was normal and the concentration of serum bilirubin was 2 mg. per hundred cubic centimeters. The patient has remained in good health.

Acute degeneration of the hepatic parenchyma in the presence of calculous obstruction of the common duct has not received the emphasis it deserves. Its severity may vary considerably. It may be mild, as in case 2, or it may be manifested as rapidly fatal acute yellow atrophy terminating within a few days after the onset of symptoms of obstruction and before surgical relief can be attempted. The depth of the jaundice, as evidenced by the concentration of serum bilirubin, is the simplest and most direct evidence obtainable. In the absence of complete obstruction of the common duct in case 2, the high value for serum bilirubin enhanced the evidence that hepatic damage was present in addition to simple obstruction. This was confirmed by the surgical observations and by the symptoms of mild hepatic insufficiency encountered in the postoperative course. As a rule, in cases of stone in the common duct the concentration of bilirubin in the serum does not rise above 10 to 12 mg. I¹ found that in 70 per cent of a series of 102 cases of stone in the common duct the concentration of bilirubin in the serum was less than 10 mg. per hundred cubic centimeters. The higher the value for bilirubin in the serum, the greater is the probability of hepatic injury. Risk of surgical intervention in these cases, if the concentration of bilirubin in the serum is 30 mg. per hundred cubic centimeters or more, especially if the bile duct is incompletely obstructed, is high. It is safer to treat the damaged liver and to await a more favorable time for intervention. On the other hand, obstruction of the duct is the primary difficulty and the sooner the obstruction can be removed without undue risk the better. Often there is considerable difficulty in evaluation of the conditions found and determination of the safest procedure. Clinical experience probably should be the final guide, but the results of liver functional tests should not be ignored.

In cases of chronic, intermittent obstruction of the common duct, hepatic changes commonly occur and likewise are of chronic nature. Usually such cases present chronic obstructive, or secondary, biliary cirrhosis. Pathologic changes are attributable to infection ascending the bile ducts. The usual manifestations are moderate enlargement of the liver and spleen, mild, persisting jaundice with acute exacerbations, pruritus and melanoderma, and these do not in themselves contraindicate surgical intervention. If such changes are not too advanced the patients usually tolerate surgical operation fairly well and often the hepatic changes undergo remarkable resolution. However, the presence of ascites or edema indicates a more advanced stage and is an unfavorable sign. In some instances the concentration of serum proteins or the colloid osmotic pressure of the blood may be fairly normal and other functional tests may present few alterations. Although some patients who present these signs also have excellent recuperative power, nevertheless our experience with such cases has not been happy.

Another form of hepatitis at times associated with calculus of the common duct is chronic atrophy or cirrhosis, often with varying degrees of "adenomatous" regeneration. This apparently is not attributable to ascending infection, because pathologically there is little evidence of ascending infection. The hepatic condition is similar to that in case 1 but the element of obstruction of the common duct also is present. Functional tests may aid materially in demonstrating the former. Even with such evidence one would hesitate to deny such patients relief of the obstruction unless clinical evidence of advanced hepatic disease is prominent.

HEPATITIS IN THE COURSE OF SYPHILIS AND ITS TREATMENT

CASE 3.—A woman aged 40 was first seen at the clinic in 1928 for deafness of seven years' duration. The liver was found to be slightly enlarged. The blood and spinal fluid were strongly positive for syphilis. A diagnosis was made of syphilis of the central nervous system. Treatment was carried out faithfully. In September 1934 tests performed on the blood gave the following results: Kline, 1+; Kahn, 1+; Hinton, positive; Wassermann (Kolmer modification), negative. Tests of the spinal fluid resulted thus: Wassermann, negative; Nonne, negative; cells, 1 lymphocyte; colloidal gold curve, 000,000,211,000,000. No treatment was given during the period from 1934 to 1936.

In January 1936 the patient returned because of an illness of three weeks' duration, characterized by impairment of appetite, fulness and distress in the epigastrium after eating, belching, nausea, occasional emesis and loss of weight and strength. The liver extended from three to four fingerbreadths below the costal margin and the spleen was palpable. Serologic tests of the blood revealed Kline, \pm ; Kahn, 2+; Hinton, positive; Wassermann, negative. The bromsulphalein test of liver function revealed retention of dye, grade 4, and the van den Bergh reaction was direct. The patient was given a high carbohydrate diet, sodium phosphate and mercury. In February she reported that her condition had improved. In April she felt and appeared much better. With the clinical improvement there was a coincident reduction of retention of bromsulphalein to grade 3, to grade 1, and finally to 0, and the van den Bergh reaction became indirect. Complete recovery ensued.

This patient had had syphilis and some enlargement of the liver for a number of years. The former had been adequately treated. The acute digestive symptoms were very suggestive of hepatic disease and functional tests confirmed the suspicion of its presence. Under treatment for hepatic disease, the woman recovered. There was no relapse in the serologic characteristics of the blood or spinal fluid in the course of this illness and the rate of recovery was more rapid than one would expect in a case of syphilitic hepatitis, judging from the amount of mercury administered. The illness was probably not due to latent toxic effects from previous therapeutic agents, for antisyphilitic drugs had not been given in the preceding two years. Furthermore, no history of the use of other hepatotoxic drugs was obtainable and there was no evidence of other systemic diseases that could affect the liver. It is my opinion that the illness of this patient was an acute degenerative lesion of the liver, of unknown etiology, and particularly not necessarily attributable to the syphilis or its treatment.

Hepatic involvement may appear in the secondary or tertiary stages of acquired syphilis. Enlargement of the liver and jaundice are common manifestations in all forms of syphilis. Since arsphenamine² has been used in the treatment of syphilis, jaundice has been more frequently observed, especially in the secondary stage. A higher incidence of acute atrophy of the liver also has been noted. Although the hepatic disease, with

1. Weir, J. F.: The Diagnosis of Jaundice: Value of Clinical and Laboratory Data, *Am. J. Surg.* 15: 494-503 (March) 1932.

or without jaundice, in the presence of active syphilis untreated or in the course of being treated, is frequently and presumptively attributable either to the primary disease or to the agents used in its control, the possibility of intercurrent and unrelated conditions of chronic or acute nature must be considered. Only recently a case of syphilis under treatment was encountered in which jaundice developed. Careful inquiry was necessary to elicit a history of cholecystitis and a subacutely inflamed gallbladder containing stones subsequently was removed. A positive serologic test for syphilis in a case of hepatic disease does not necessarily mean that the condition of the liver is due to syphilis. Other evidence usually is necessary. Such evidence, however, often is not obtainable or may become available only at necropsy.

HEPATITIS WITHOUT JAUNDICE

Jaundice is the symptom which leads all others in calling attention to the presence of hepatic disease. In absence of this symptom the occurrence of an enlarged liver or spleen, ascites, pruritus and hematemesis also serve to direct attention to the liver. However, there are many cases of hepatic disease wherein none of these conditions are present. The condition, in such cases, may spring from various diseases or toxins but in many the etiology is unknown. Comfort and I² have reported cases of hepatic disturbance attributable to cinchophen wherein jaundice was absent. Numerous similar cases subsequently have been encountered. The use of hepatic functional tests has aided materially in their recognition and in the institution of protective measures. Likewise these tests, judiciously used in examination of the syphilitic patient who is under arsphenamine therapy, have disclosed development of hepatic injury in its earlier stages. The occurrence of hepatic involvement in fatal cases of pernicious vomiting of pregnancy long has been recognized but it remained for tests of hepatic function to demonstrate the common occurrence of various degrees of disturbances of the liver in the less severe cases. It is also known that fatal acute atrophy of the liver may occur without the development of jaundice. The changes in the liver in the presence of severe anemia have been emphasized by Rich.³ Recently, Snell and Comfort⁴ have described cases of presumably fatty degeneration of the liver without jaundice, associated with extreme atrophy of the pancreas. Involvement of the liver in cases of exophthalmic goiter has been described by numerous authors. The cases of Beaver and Pemberton⁵ were severe and the outcome was fatal. It is not so well recognized that minor degrees of hepatic disturbance may occur in milder cases of exophthalmic goiter, although Bartels⁶ has found frequent disturbances of the liver in such cases, using the hippuric acid test. At the clinic, however, we prefer to depend on the bromsulphalein test in those cases in which jaundice is absent.

A number of cases of hepatic disease without jaundice, unassociated with other diseases and of unknown etiology, have been encountered. Although these have

been discussed in detail elsewhere,⁷ I present one as illustrative of the group:

CASE 4.—A man aged 34 was seen repeatedly between 1932 and 1934 for duodenal ulcer and sinusitis. In March 1934 resection of the stomach was done with excellent results. The liver was grossly normal. In December 1936 the man returned because of periumbilical distress of two months' duration associated with insomnia, anorexia, marked nausea and loss of 10 pounds (4.5 Kg.). Physical examination revealed no abnormalities. Retention of bromsulphalein was graded 4. The van den Bergh reaction was direct; the concentration of serum bilirubin was 1.6 mg. per hundred cubic centimeters. On a high carbohydrate diet and daily intravenous administration of dextrose solution, the patient's condition gradually improved. Coincidentally, retention of bromsulphalein declined; it was graded 3, 2, and subsequently 1, in the two weeks following the patient's admission. Another four weeks elapsed before the patient fully recovered. Examination one year later showed him to be in good health.

The occurrence of anorexia, nausea, vomiting and epigastric distress brought the liver under suspicion. The absence of jaundice or hepatic enlargement necessitated the employment of hepatic functional tests for confirmatory evidence. The severity of the symptoms and the laboratory observations indicated a rather severe lesion of the liver. Improvement in the laboratory appearances coincided with the clinical improvement. Etiologically, evidence of any known exogenous or endogenous toxic agent could not be demonstrated and the case must be considered one in which the hepatic condition was of unknown origin. The normal condition of the liver at the previous exploration, and the course of the later illness, would seem to indicate that the acute hepatic injury underwent complete resolution.

In a few cases slight enlargement of the liver directed attention to the possibility that it had undergone pathologic change. In other cases, indefinite or extremely mild symptoms were present and the laboratory investigation was made in an effort to find an explanation for some of them. In further cases, symptoms were more severe and suggestive of hepatic disease and functional tests indicated hepatic changes. In the milder cases, definite, active therapy did not seem indicated. However, subsequent avoidance of hepatic toxins was counseled. In the more severe cases, more active therapy was needed. In these, the standard, high carbohydrate, diet supplemented by intravenous administration of dextrose solutions when necessary proved adequate. The pathologic changes were conjectural, material for biopsy was not available, and fortunately the need for necropsy did not arise. Presumably the changes were degenerative processes or some degree of necrosis of the hepatic cells. Prognosis also was uncertain. In cases in which there was some enlargement of the liver chronic changes probably were present; exacerbations probably were in progress at the time of our observations. Similar exacerbations may occur in the future. In other instances there is every reason to believe that the illness was acute, although of varying degree of severity, and that recovery was complete.

FUNCTIONAL TESTS

In the presence of jaundice the measurement of the concentration of bilirubin in the serum furnishes information of utmost importance. The highest levels (from 30 to 50 mg. per hundred cubic centimeters) are found in association with acute, severe, hepatogenous forms

2. Weir, J. F., and Comfort, M. W.: Toxic Cirrhosis Caused by Cinchophen, *Arch. Int. Med.* 52: 685-724 (Nov.) 1933.

3. Rich, A. R.: The Pathogenesis of the Forms of Jaundice, *Bull. Johns Hopkins Hosp.* 47: 338-377 (Dec.) 1930.

4. Snell, A. M., and Comfort, M. W.: Hepatic Lesions Presumably Secondary to Pancreatic Lithiasis and Atrophy: Report of Two Cases, *Am. J. Digest. Dis. & Nutrition* 4: 215-218 (June) 1937.

5. Beaver, D. C., and Pemberton, J. deJ.: The Pathologic Anatomy of the Liver in Exophthalmic Goiter, *Ann. Int. Med.* 7: 687-708 (Dec.) 1933.

6. Bartels, E. C., and Perkin, H. J.: Liver Function in Hyperthyroidism as Determined by the Hippuric Acid Test, *New England J. Med.* 216: 1051-1060 (June 17) 1937.

7. Weir, J. F.: Atrophy and Necrosis of the Liver Without Jaundice, unpublished data.

of jaundice and cases of neoplastic biliary obstruction. In cases of incomplete obstruction, high readings (20 mg. or more per hundred cubic centimeters) indicate definite parenchymal involvement of the liver. Fluctuations in such cases are not as frequent as they are in the more common degrees of icterus from intermittent obstruction. However, after a considerable period slow decline may occur. This would indicate a tendency to partial recovery from the hepatic injury. The longer the high level is maintained, the more severe is the injury and the slower will be the decline of the concentration of serum bilirubin.

In the absence of jaundice, determination of the excretory function of the liver by the rate of excretion of various dyes yields most important information. In general, in these cases, the degree of retention of dye can be taken at its face value. Even slight retention of dye is significant. Retention occurs in a wide variety of primary hepatic diseases, in many of which high degrees of retention are indicative of an unfavorable prognosis. Hepatic involvement often can be demonstrated in a number of other conditions, such as exophthalmic goiter, toxemia of pregnancy, amyloidosis, poisoning from various hepatotoxic substances such as cinchophen and arsenic, many of the infectious diseases, and the infiltrations of malignant and leukemic processes. In other instances, such as in case 4, hepatic involvement may be demonstrable in the absence of associated diseases and clinical evidence of hepatic disease may be minimal. Lessening of the degree of retention usually parallels clinical improvement.

Hypoglycemia has been noted experimentally in hepatic injury from various toxins, and occasionally in a variety of clinical hepatic diseases. However, the glycogenic function seems well maintained as a rule, to the end. Other functions tend to fail first. For this reason, functional tests of carbohydrate metabolism have been disappointing in practice. The galactose tolerance test has had a greater vogue than others in clinical medicine. The test has been used to distinguish intrahepatic from obstructive jaundice, by obtaining positive results in the former, but we have not been able to confirm this use of the test. Thus, in our hands the test has been consistently negative in portal and biliary cirrhosis and positive in from 25 to 40 per cent of cases of obstructive jaundice.

In acute hepatic disease, such as yellow atrophy, the blood amino acid may be increased, the urea may be decreased and tyrosine may appear in the urine. The liver has been shown to be important in maintaining the normal level of serum proteins. Lowering of these has been noted frequently in experimental and clinical hepatic disorders, especially in instances in which edema or ascites was present. Reversal of the albumin-globulin ratio not infrequently is encountered. Lowering of the colloid osmotic pressure also may occur and, as Butt and Keys⁸ have shown, does not necessarily parallel lowering of the serum protein.

Fatty changes in the liver and alteration of the blood lipids occur in many experimental and clinical conditions. Extensive fatty changes have been noted to occur in depancreatized animals. Similar clinical instances of presumably fatty liver in cases of extensive chronic pancreatic disease have been noted. In obstructive jaundice, cholesterol and cholesterol esters in the

blood are frequently increased; in some instances of chronic obstruction these are extremely high and fail to return to normal even after relief of the obstruction, thus indicating permanent hepatic damage. In parenchymatous hepatic disease a marked decrease of cholesterol and cholesterol esters is noted at times. Cholesterol esters may entirely disappear from the blood in the more severe cases of this type and may be indicative of an unfavorable prognosis. Other disturbances of lipid metabolism include a lowered output of cholesterol in the bile and lipemia. Riegel, Ravdin and Rose⁹ have shown the prognostic import of low output of cholesterol in bile drained from the common duct. Occasionally we have encountered arterial lipemia in the terminal stages of chronic hepatitis and we encountered venous lipemia in a case of splenic anemia following splenectomy.

Of the tests of the detoxifying function of the liver, the one based on the ability of the liver to conjugate benzoic acid and aminoacetic acid to form hippuric acid has best stood the test of clinical evaluation. In a case without jaundice the results parallel closely those of the bromsulphalein test, while in a case in which jaundice is present they correspond, in a general way, to the degree of hepatic injury noted at operation or necropsy. In "surgical" types of icterus it has been found that values of less than 1.5 Gm. were associated with an unfavorable prognosis. In case 1 the low results indicated hepatic disease.

A study of the bile discharged from the drainage tube in surgical cases also offers valuable information of the functional capacity of the liver. Marked cholorrhea indicates an unfavorable course. Gray and McGowan¹⁰ have demonstrated the significance of lowering of the bile salt output. Amounts less than 100 to 200 mg. per hundred cubic centimeters of bile indicate extensive hepatic damage and, frequently, a fatal prognosis.

Because of the many functions of the liver, many tests of its function have been developed; and, while no one test gives complete or perhaps significant information on how the liver is functioning in a given instance, the use of several gives more accurate knowledge of its condition. Some tests are more applicable in some cases than in others. Positive results are particularly significant in demonstrating advanced changes. By the use of functional tests, progress is being made in the study of clinical cases and in knowledge of the pathologic physiology of the liver. Such studies may definitely incriminate the liver in various diseases wherein hepatic involvement may occur but is unsuspected. When such involvement of the liver has been demonstrated, the degree of alteration of the functional tests may be indicative of the extent of such involvement, its course and its prognosis.

SUMMARY AND CONCLUSIONS

In this discussion I have attempted to point out some forms of hepatitis not commonly recognized, namely (1) chronic hepatitis either masquerading as stone of the common duct or in association with calculous cholecystitis, and the acute and chronic degenerative hepatic lesions which may accompany stone of the common bile duct; (2) hepatitis occurring in the course of syphilis and its therapy; (3) hepatitis of several types without jaundice. In cases of the first group, diagnosis

8. Butt, H. R., and Keys, Ancel: Colloid Osmotic Pressure: Studies of Normal Individuals and of Those with Hypoproteinemia, *Proc. Staff Meet., Mayo Clin.* 12: 566-570 (Sept. 8) 1937.

9. Riegel, Cecilia; Ravdin, I. S., and Rose, H. J.: Cholesterol in Human Liver Bile, *Am. J. M. Sc.* 193: 446-447 (March) 1937.
10. Gray, H. K., and McGowan, J. M.: Liver Damage in Biliary Disease: Its Relation to the Concentration of Bile Acids in the Bile, *Proc. Staff Meet., Mayo Clin.* 12: 196-199 (March 31) 1937.

often is uncertain until exploration is undertaken. However, the presence of unusual symptoms such as unexplained weakness, loss of weight, dyspnea and edema may arouse suspicion that the liver is of more importance than the cholecystic disease or the condition of the rest of the biliary tract in explaining the patient's illness. Hepatic and splenic enlargement are indicative of long-standing disease. Chronic jaundice and ascites are also important signs of extensive disorganization of the liver. Intense jaundice (high levels of serum bilirubin), especially in the absence of complete ductal obstruction, indicates acute hepatic damage. This may manifest itself in such a serious form as acute yellow atrophy. An attitude of constant suspicion of the possible presence of hepatitis is necessary in recognition of many of these states. Hepatic functional tests, particularly determination of the serum bilirubin, the galactose tolerance, the excretion of hippuric acid and the concentration of cholesterol and protein in the blood in the presence of jaundice and determination of the rate of excretion of bromsulphalein in the case without jaundice, offer much assistance. Although these tests may present positive evidence, the disposal of such cases will rest largely on clinical grounds. Knowledge of the value and interpretation of such tests has not progressed to the stage of infallibility and, on the basis of their results, patients cannot justly be denied their only chance of cure or even of palliation. However, positive tests give better evaluation of the risk and indicate that adequate time should be taken for thorough preoperative preparation.

Acute hepatitis in association with syphilis and its treatment usually is readily recognized and often is attributable either to the primary disease or to its therapy. However, the possibility of independent lesions cannot be ignored and difficulty may be encountered in the absence of jaundice. Laboratory procedures may aid in confirmation of suspicions.

A variety of causes may give rise to disorders of the liver without jaundice. Many such cases and their etiologic factors are readily recognized, but there are unusual cases, unassociated with other diseases and of unknown etiology. The bromsulphalein test for hepatic function has been particularly valuable in recognition of these cases and as an indication of improvement. Anorexia, epigastric distress, nausea and, at times, vomiting have been prominent symptoms and, unless otherwise explained, such a syndrome should direct attention to the liver.

ABSTRACT OF DISCUSSION

DR. DWIGHT L. WILBUR, San Francisco: This paper calls attention to the value of certain tests of hepatic function when they are viewed in the light of clinical observations. The symptoms of hepatitis with the exception of jaundice and of an enlarged and tender liver are nonspecific, for one may observe upper abdominal colics, nausea and vomiting, pruritus, hematemesis, anorexia, epigastric distress and loss of weight and strength and discover an enlarged spleen, ascites or melanoderma in the absence of disease of the liver or biliary tract. If these symptoms are present or if such observations are made one may suspect the presence of hepatic disease, and the use of certain tests of hepatic function may aid in substantiating or establishing the diagnosis. One should not gain the impression that tests are required if accurate determination and interpretations and degree of hepatic derangement. In the first place considerable familiarity and experience with the technic of some of the tests is required if accurate determination and interpretations are to be made. In the second place clinicians with much experience in the use of these tests will recall instances in

which certain of them yielded results within normal limits in cases in which there was marked hepatic disease. For many clinicians the value of hepatic function tests lies principally in the fact that they establish a measure of the degree of hepatic damage in a case in which hepatic involvement is suspected clinically and that thereby is established a base line by which the preoperative or postoperative course and progress of hepatic function and disease may be more closely followed. For those who do not have access to a laboratory in which some of the more difficult tests for hepatic function can be carried out, observations of the intensity of the jaundice, of its duration, of its course (particularly whether it is fluctuating or constant) and observation (by means of the duodenal tube) of the presence of or absence of a flow of bile into the intestine will prove useful. Indeed the three most useful facts to be used in the differential diagnosis of patients with jaundice are the occurrence or absence of pain, the presence or absence of a flow of bile into the duodenum, and the degree and course of the jaundice. I am interested to know Dr. Weir's opinion of the value of determinations of total cholesterol and cholesterol esters of the blood, of the Takata-Ara test and of the phosphatase content of the blood as measures of hepatic function.

DR. SIDNEY A. PORTIS, Chicago: Many gastro-enterologists but too few clinicians realize the role of the liver in the metabolism of the body. We have just heard a good discussion of liver function, and yet all we know at present is that dextrose will help liver diseases. It seems that practically all the functions of the liver are dependent on the glycogenic content of the liver cell. When the liver is damaged it takes a higher concentration of sugar in the blood to reach the liver cell because the threshold in the liver is raised. One should necessarily question then whether or not there can be sufficient absorption of dextrose from the gastrointestinal tract in amounts that would be beneficial to a damaged liver. It would seem more logical to give dextrose intravenously so that the concentration of sugar in the blood reaching the liver at any one time would be sufficient to overcome the raised liver threshold for its utilization. Many physicians do not appreciate the so-called subhepatic states in which patients complain of lethargy, weakness and swelling. These are probably associated with hypoglycemic manifestations, which are dependent on the glycogenic function of the liver. I have been giving these patients 50 cc. of 50 per cent dextrose solution daily without insulin. I use insulin only when there is evidence of a diabetic component to the clinical picture. Some of the most marvelous results of intravenous dextrose therapy may be seen at times in cases of so-called atrophic cirrhosis of the liver. If the liver is not too badly damaged and beyond any repair, one may frequently see, after the daily intravenous injection of dextrose, a gradual but definite improvement in the clinical picture. Many of these patients do not have to be given paracentesis. Frequently the hemorrhages from the esophageal varices subside, and those patients who were relegated to the "junk heap" in the past have been able to regain their near normal status, gain in weight and for the most part become very comfortable.

DR. EDGAR WAYBURN, San Francisco: I have seen several cases of cirrhosis of the liver in which it was possible to make the diagnosis before jaundice developed. Three years ago I had the opportunity to observe one of these cases pathologically. In this case there was an acute inflammatory reaction and necrosis of liver cells in irregular zones having no constant relationship to the liver lobules. A similar type of reaction occurs in hepatic cirrhosis. In this case, however, there was a barely detectable amount of fibrosis. I tried without success to find similar cases in the literature. I believe that the signs which may be of value in such cases include nausea, vomiting, epigastric and right upper quadrant discomfort, weakness, a large and often tender liver, and impaired liver function, as Dr. Weir has pointed out. With regard to the differential diagnosis of gallbladder disease and cirrhosis, with Dr. Cherry at the San Francisco Hospital I have now used the Takata reaction in a series of almost 1,500 cases and in a number of instances have found that it was a very valuable laboratory aid in the differentiation of these two diseases. It is a test which in our series has been positive in 90 per cent of cases of cirrhosis of the liver and uniformly negative in gallbladder disease.

DR. JAMES F. WEIR, Rochester, Minn.: In reply to Dr. Wilbur's questions concerning the value of cholesterol and cholesterol esters and the phosphatase and Takata-Ara tests, it would take too much time to attempt an adequate answer. My experience has been similar to that of the Mount Sinai group with regard to the cholesterol and cholesterol esters. I have discontinued using the Takata-Ara test. The phosphatase has been helpful in some cases but there have been many exceptions. Dr. Portis seemed favorable impressed with the results of treatment in some of these advanced cases of cirrhosis or other hepatic disease. I think this is justifiable in certain cases. Judging from the wrecks that one sees, certain of them definitely can be rehabilitated. As these occur infrequently, however, one becomes discouraged at the bad results one gets in cirrhosis as a group. In closing, I want to emphasize in particular the last group of patients, with acute symptoms in the absence of jaundice, who have functional disturbances and usually recover.

COCCIDIOIDOMYCOSIS

THE PRELIMINARY ACUTE INFECTION WITH FUNGUS COCCIDIOIDES

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Since coccidioidal granuloma has been found to be of considerable frequency in California, particularly in the San Joaquin Valley,¹ and since it has been found that not only man but cattle and sheep may acquire the disease,² there has been much interest in how infection with the fungus *coccidioides* may be acquired. It has been shown that occasionally infection occurs first at the site of a break in the skin such as a puncture of a cactus spine³ or an abrasion from picking walnuts,⁴ but such a traumatic history has rarely been obtained. Clinical experience has shown that there is no indication of man to man or animal to man infection, and study of other possible methods of infection, including insect bite, have failed to show how the disease is transmitted. A number of clinicians have long suspected that the infection may follow inhalation of the infecting organism, but this has necessitated their disregarding the parasite as it occurs within the animal body, the endosporulating spherules, and has made it necessary to consider whether some element of the vegetative phase of the fungous growth might be the infecting agent.

Beginning with Dr. Ophüls,⁵ a few investigators, including Wolbach,⁶ MacNeal and Taylor⁷ and Ahlfeldt,⁸ have worked with *coccidioides* fungus, and all have recognized that the method of reproduction in the vegetative phase is by chlamydospores, organisms which usually have not been studied by clinicians because the clinician sees only the patient, and the endosporulating spherules, the cycle of reproduction within the tissues of the patient, are the only reproductive elements met in the parasitic phase of *coccidioides* activity. It has

seemed possible to some investigators that the chlamydospores of the vegetative phase might be the infecting organism which can be inhaled. In 1929 Ophüls⁵ while discussing the case report of Pulford and Larson⁹

All evidence so far gathered seems to point to respiratory involvement with primary localization of the virus in lung. . . . It is probably the spores of the fungus grow that become mixed with dust and are then inhaled into lungs. The finding of the disease in animals such as cats and sheep does not seem to me to suggest that the infection from animals to human beings. It is much more likely that the animals contract the disease much in the same way as human beings do in the infected region.

Proof that the inhalation of chlamydospores may cause *coccidioides* infection was established by an accident in our laboratory.¹⁰ A young man who was commencing work with *coccidioides* fungus inadvertently opened an old petri dish culture which he proposed to use. When the cover glass of the petri dish was removed he noted a fine cloud arise from the old culture. Nine days later he became ill with a symptom complex which has been found to be common in the San Joaquin Valley, Calif., the region in which approximately 90 per cent of the known cases of coccidioidal granuloma in the United States have originated. Like the great majority of patients in the San Joaquin Valley, the young man recovered without complications, and he is now apparently well, nine years later. Shortly after this case, another young man, from near Bakersfield in the San Joaquin Valley, was under the care also of Dr. H. Pierson, suffering from a similar illness. The main difference between the two cases was that there was an outbreak of erythema nodosum in the first case but not in the second. In both cases cultures of sputum gave a growth of fungus *coccidioides* which was proven virulent by guinea pig inoculation. Like the first patient the second young man recovered promptly from his acute illness.

It has been found that a symptom complex like that of the first of these patients is common in the San Joaquin Valley; so common, in fact, that it is popularly known as "valley fever" or "desert fever." Persons of all ages and of either sex may be affected; they are usually ill from three to six weeks, and the most of them recover without having had any complications. Many apparently are not sufficiently ill in the beginning to call for medical aid; as a matter of fact, it is often the erythema nodosum which brings them to a physician. In a questionnaire sent to the practicing physicians in the San Joaquin Valley, seventy-five physicians report that they had seen 354 patients with valley fever erythema nodosum between Jan. 1, 1936, and May 1937, of whom 353 had recovered without complications and one had died of coccidioidal meningitis.

At the onset of acute illness the patient usually describes it as a bad cold or "flu." He complains of feeling bad, with headache and often general aches and pains. Sometimes the aches and pains are particularly severe about the chest, and the patient complains of pleurisy; a number of such patients have had their chest strapped with adhesive tape. At times there are indigestive gastrointestinal disturbances. Frequently there is a mild sore throat which is called tonsillitis. Occasionally there is some conjunctivitis with bulbar hyperemia, but rarely are phlyctenulae seen. Sometimes there is

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2. Beck, M. Dorothy: Proc. Soc. Exper. Biol. & Med. 26: 534 (March) 1929.

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9. Pulford, D. S., and Larson, E. E.: Coccidioidal Granuloma, J. M. A. 93: 1049 (Oct. 5) 1929.

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rapid loss of as much as 15 or 20 pounds (7 or 9 Kg.) in weight. Fever may begin at the onset or four or five days later. Not infrequently the temperature is no higher than 100 F., but sometimes, when there are signs of severe bronchitis or bronchopneumonia, it may be 104 or even 105 F. Occasionally a patient has an early chill and he may have sweating, but the incidence of chills and sweating is not constant.

There is early bronchitis, sometimes with unproductive cough, but varying amounts of mucopurulent sputum are common. Sometimes the duration of cough with sputum is very short but at other times the duration of the cough is longer, and the amount of sputum may be large and it may be streaked with blood. Often the patient feels better after a few days and thinks he is getting well, but in from eight to fifteen days after the onset erythematous nodules develop in the skin; these are popularly described as "the bumps." They are typically those of erythema nodosum on the shins but when they occur elsewhere are sometimes described as erythema multiforme. It is only after the occurrence of "the bumps" that the disease is known as valley fever or desert fever.

The nodules of erythema nodosum usually appear primarily on the shins, where they are most numerous. They may occur also on the thighs, buttocks, arms, upper part of the chest and scalp. They do not fluctuate or suppurate but may be fiery red and very tender or painful. It is often the pain of the erythema nodosum which brings the patient to a physician. Within from forty-eight to seventy-two hours the nodules begin to change from fiery red to purplish and to fade. They have usually disappeared in from four to five days except for a brownish pigmentation of the skin, which may persist for several weeks after the tenderness and swelling have disappeared. Occasionally, but rarely, there are recurring attacks of erythema nodosum during a single illness.

If roentgenograms of the chest are taken during the acute attack, dense shadows will usually be found in the hilar regions, indicating enlargement of the hilar glands. Radiating from the hilar region and more widely distributed through the lung area are densities indicating parenchymatous involvement in various parts of the lung; these may occur in all the lobes. A roentgen diagnosis of tuberculosis is often made on the first examination, but as time goes on the areas of increased density gradually clear up until, after a few weeks, the lungs may appear entirely clear. Not infrequently the roentgenologist states the conclusion that the condition could not have been tuberculosis because the lungs cleared so promptly. Occasionally a patient with such pulmonary shadows has been sent to a sanatorium for tuberculosis when it was impossible to prove tuberculosis by recovering acid-fast bacilli or by tuberculin tests.

When sputum from a patient with valley fever is examined it is usually impossible to find acid-fast bacilli, although patients have been known to have both coccidioides infection and tuberculosis. Not infrequently, however, all that is found is the spherules of the coccidioides type with culture of fungus coccidioides, and coccidioidal granuloma in injected guinea pigs. Seventy-two of 112 specimens of sputum which were sent to our laboratory from the San Joaquin Valley have proved positive for coccidioides infection. In only four were tubercle bacilli found. It is not yet known how early in the disease the coccidioides fungus may

be found in the sputum or how long it may persist, although it is known that it may disappear before the output of sputum is discontinued. It should be remembered that, as in tuberculosis, the infecting organism may be recovered by washing the stomach of a child who is too young to raise sputum. We have studied several such cases,¹¹ and the typical spherules were seen in the mucopurulent sputum recovered by lavage, cultures showed growth of fungus coccidioides and the organism was proved virulent by guinea pig inoculation.

Examination of the urine shows nothing different than is usual in the case of febrile conditions. The leukocyte count varies from about normal to 15,000 but often, associated with the erythema nodosum, there may be eosinophilia. The highest eosinophil count we have seen was that of a patient whose leukocytes varied from 8,000 to 13,500; there were 4 per cent eosinophils on admission, 16 per cent on the eighth day of illness and 4 per cent again on the eleventh day. We have had opportunity of making sedimentation tests on three patients and found values of 31 mm., 32 mm. and 45 mm., respectively, in sixty minutes.

The use of the coccidioidin cutaneous test in cases of valley fever has been most helpful in correlating the diagnosis with coccidioides infection. It has been found that the reaction in cases of valley fever is much more violent than in cases of coccidioidal granuloma. As a matter of fact, the size of the dose for intradermal injection was stated by Jacobson¹² to be 0.3 cc. of the undiluted filtrate, which he prepared for diagnosis of coccidioidal granuloma, but such a large dose has proved entirely too strong for valley fever. It may cause immense edema and necrosis of the skin in cases of acute involvement. We have found that 0.1 cc. of a 1 to 1,000 dilution of coccidioidin which we have prepared is adequate and produces well marked reactions, sometimes with vesicle formation in cases of primary infection. At least 0.1 cc. of a 1 to 10 dilution of this coccidioidin is necessary for coccidioidal granuloma. This corresponds to the experience of Wallgren¹³ with tuberculin in the case of primary tuberculosis. He reported that among children with erythema nodosum accompanying primary tuberculosis the sensitivity to tuberculin may be so high as to cause a reaction to 0.000001 mg., whereas only three of 321 tuberculous children without erythema nodosum were sensitive to 0.001 mg.

However, there are also cases of primary coccidioides infection which differ only in the fact that there is no erythema nodosum, and they are therefore not considered cases of valley fever. It has been found that in these cases too there may be fungus coccidioides in the sputum, and there may be prompt recovery from the acute illness. The diagnosis may be bronchopneumonia or influenza, and, as with valley fever, the condition may go on to typical coccidioidal granuloma. We have seen two such cases in which recovery occurred and have records of several in which coccidioidal granuloma developed, as well as records of several in which coccidioidal granuloma developed after erythema nodosum. At the present time there is no knowledge as to how frequently the acute infection may occur with or without erythema nodosum or as to whether either type is apt to be followed by coccidioidal granuloma more often than the other.

11. Dickson, E. C.: *California & West. Med.* 47: 151 (Sept.) 1937.

12. Jacobson, H. P.: *Fungous Diseases*, Springfield, Ill., Charles C. Thomas, Publisher, 1932, p. 255.

13. Wallgren, Arvid: *Lancet* 1: 359 (Feb. 12) 1938.

It is therefore definitely established that infection with coccidioides fungus is caused by the chlamydo-spores of the vegetative phase of the fungus, which in some way gain access to the tissues. There seems to be no doubt that the chlamydo-spores are carried through the air, presumably associated with dust. When primary cutaneous lesions follow trauma of the skin, such as a prick of the skin by a cactus spine or an abrasion of the skin caused by picking walnuts, undoubtedly the chlamydo-spores are associated with the dust on the offending objects. In general, however, primary coccidioides infection seems to be acquired by inhalation of the chlamydo-spores, and the development of the primary lesions is in the lungs or the regional lymph glands. Thus can the occurrence of coccidioides lesions in animals in the endemic areas as well as in man be rationally explained. The development of the later coccidioid granuloma is undoubtedly secondary and is caused by migration of the virus to different parts of the body from the primary foci in the lungs or peribronchial lymph glands, presumably by the blood stream.

It follows therefore that infection with coccidioides fungus may be manifested in at least two ways: by a primary acute infection of the respiratory tract, often accompanied by erythema nodosum, from which the great majority of patients recover without complications, and by a later more or less chronic granulomatous disease, known as coccidioid granuloma, which may be very disabling and which has a case mortality rate of approximately 50 per cent. It is therefore necessary to have a name for coccidioides infection to include both types of illness. In a previous report¹¹ I suggested the term coccidioidomycosis, which may be classified as primary for the acute initial infection and progressive or secondary for the stage of coccidioid granuloma. The latter classification may be subdivided to indicate the regional distribution of the lesions if desired; for instance, of the skin, bone, meninges, lungs and so on.

SUMMARY

The preliminary illness caused by infection with fungus coccidioides has been recognized.

The disease is caused by inhalation of the chlamydo-spores, which are formed in the vegetative phase of growth of the fungus.

It is a form of infection of the respiratory tract, in many cases accompanied by erythema nodosum, and the great majority of patients recover promptly without complications.

The incidence of erythema nodosum is very high but not constant. When this condition occurs the disease is known in the San Joaquin Valley as "valley fever" or "desert fever."

The acute illness, whether or not there is erythema nodosum, may progress to coccidioid granuloma.

ABSTRACT OF DISCUSSION

DR. K. F. MEYER, San Francisco: I call this presentation the renaissance period of coccidioidomycosis. All have been interested in this disease for many years; from an epidemiologic standpoint the available story didn't fit. How could a disease have 98 or 99 per cent mortality? Anybody who thinks biologically was aware that doubtless coccidioid granuloma was merely the end result of a disease which masqueraded under an entirely different picture. Dr. Dickson has opened the door to let us look into this exceedingly complex problem. Since Coccidiomyces is not transmitted from host to host and does not behave as a true parasite along infection chains, one has to ask: Is it a pathogenic saprophyte and does this patho-

genic saprophyte acquire later parasitic properties? If so, what types of poison does it produce and what is the pathogenesis? I could mention an unlimited number of questions which doubtless Dr. Dickson and his associates are going to answer, but a few I should like to point out because we are here in a public health section. In the first place, the infection in California is aerogenic; the lung is the portal of entry. It therefore can occur only in regions where the atmospheric conditions favor the dissemination of the chlamydo-spores in the dust. It is interesting that by contrast the paracoccidioidomycosis of Brazil, recognized many years ago and carefully studied by Almeida, is apparently not aerogenic. In a tropical climate dust infections are infrequent. The North American coccidioidomycosis apparently is primarily a pulmonary infection with secondary distribution along the hematogenic route, while the South American type is a local process with primary distribution in the buccal cavity—tonsillar invasion and infection of the tongue and intestine. Of the total number of cases, over 280, that came to autopsy in Brazil, only about 15 per cent showed pulmonary lesions, which to all intents and purposes were decidedly secondary. I wish to stress these interesting biologic differences. Next I should like to call attention to the possibility which is reasonable to suspect, that, since we are dealing with a saprophytic fungus, we might find a great variety of Coccidiomyces, varieties from the standpoint of biology and their behavior toward the host. Just as in the field of sporotrichosis at least three varieties have been recognized and in the field of toxicogenic saprophytes, such as botulisms, five types have thus far been reached, A, B, C, D and E, I shouldn't be surprised if the rest of the alphabet would be fulfilled if every section of the world should be searched. These considerations raise the question Should the antigens which are to be used in the allergic tests, like the coccidioidin, be made from one strain or should a polyvalent preparation be used? We should not perhaps let our interest be entirely directed in analyzing the parasite, but we must study the factors which influence the host.

DR. KENNETH H. ABBOTT, Ontario, Calif.: I have a word to add in expressing our compliments to Dr. Dickson for the work presented here. Those of us interested in neurology occasionally see one particular type of this disease that is not generally recognized. I refer to the "primary coccidioid meningitis." Although it is at times possible to find in the history and the autopsy a previous infection, more often none is evident and no primary focus is found at autopsy. Most of these patients come to the neurologist because of just headaches, of symptoms of brain tumor or of meningitis and finally die after from three months to a year without a correct diagnosis unless the organisms in the spinal fluid are found or, as in one of our cases, a suboccipital exploratory craniotomy is done to make the diagnosis. We have been studying this type of occult coccidioid infection at the Cajal Laboratory of Neuropathology (Los Angeles General Hospital) and have corroborated Dr. Dickson's finding of eosinophilia in the blood and have also found in one instance a 15 per cent eosinophilia in the spinal fluid. I would mention one other diagnostic point: in cases of unknown type of meningitis, the skull should be roentgenographed. If small, punched-out areas are found, one should beware. It may be coccidioides. We have found that to be so in several instances.

DR. ERNEST C. DICKSON, San Francisco: In reply to the question of Dr. Abbott, I have been attempting to learn something about the incidence of the acute symptoms in the cases of coccidioid granuloma which have recently been reported. Of course, in trying to get the early history of patients who died and came to autopsy some time ago, little success has been achieved as a rule. However, among the cases that came to autopsy during the past year it was found that thirteen had initial symptoms of what could be called "flu," three diagnosed as pneumonia and three with indefinite histories from which no tentative diagnosis could be made. Of the seventeen patients who died, six had coccidioid meningitis, some of which corresponded with an acute illness in which an early diagnosis of meningitis had been made although, in some, diagnosis of coccidioid infection was not recognized before the patient was out of bed because of the primary illness. The fact that no primary lesions were diagnosed at autopsy does

not seem to me to indicate that there need be any other suspected method of causing the lesions in the meninges than is known, to occur so often. As Dr. Meyer stated, there are many questions which he would like to have settled. I have thought of many but undoubtedly not all of them. At present a rather satisfactory field investigation is in progress in the San Joaquin Valley that is resulting better than might have been expected. However, there remains much to learn about this disease, considered particularly from the standpoint of how it begins rather than from the standpoint of what eventually happens.

DECOMPRESSION OF THE SMALL INTESTINE IN THE TREATMENT OF INTESTINAL OBSTRUCTION

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DETROIT

The role of distention as an important factor in the initiation of conditions which lead to a fatal outcome of intestinal obstruction has been well demonstrated within the last few years. The work of Ward¹ and of Wangensteen^{1a} with respect to the beneficial effects of gastric or duodenal suction is based largely on the proposition that with relief of distention not only does the patient become more comfortable but in many cases the release of tension above the obstruction permits passage of the intestinal contents through the narrowed lumen of the bowel. The role of distention in the initiation of vomiting, the common precursor of loss of fluid and salt in cases of intestinal obstruction, has been well studied by Herrin and Meek.² These authors pointed out that it is possible to produce the symptoms and sequelae of intestinal obstruction in animals by distention even though obstruction is not present.

Beneficial effects from enterostomy in cases of intestinal obstruction likewise attest the efficacy of decompression of the distended bowel in the control of intestinal obstruction. Enterostomy when it decompresses the bowel directly above the site of obstruction is a surer method than is gastric or duodenal suction, but the operation entailed frequently negates this advantage.

With encouragement from the assistance offered by gastric or duodenal suction after the method of Wangensteen in the treatment of intestinal obstruction and the knowledge of the technic and possibilities of intubation of the small intestine, Dr. William Osler Abbott and one of us prepared to pass a tube into the small intestine of a patient with intestinal obstruction who had refused operation. The tube passed with greater ease than we had anticipated, and decompression of the distended intestine was effected.

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1. Ward, Robertson: *Am. J. Surg.* 8:1194 (June) 1930.

1a. Wangensteen, O. H.: *Therapeutic Considerations in the Management of Acute Intestinal Obstruction*, *Arch. Surg.* 26:933 (June) 1933.

2. Herrin, R. C., and Meek, W. J.: *Distention as a Factor in Intestinal Obstruction*, *Arch. Int. Med.* 51:152 (Jan.) 1933.

A certain amount of rationalization was necessary to enable us to proceed with the treatment of intestinal obstruction by the use of intestinal intubation. The question of the efficacy of the method was of no great concern, since we had clearly demonstrated that even when a patient was vomiting the contents of the small intestine the tube would pass down the small intestine to the cecum and the contents of the small intestine removed from just above the point of obstruction, the site of election for an effective enterostomy. This procedure in effect was tantamount to an enterostomy without the trauma of an operation.

However glowing the possibilities seemed, other factors gave us concern. The likelihood that the period consumed in passing the tube might be valuable time lost to the patient appeared important. With the tube placed in the stomach or duodenum, suction could be applied and would then be as effective as the form of early preoperative care to which we had become accustomed since the popularization of suction drainage by Wangensteen and Paine.³ This treatment should be instituted while fluids are administered even though early operation is contemplated. The further passage of the tube might require hours, but if the patient was watched carefully for the development of untoward signs, this did not need to be of any great moment in the majority of instances. Subsequent experience has strengthened our point of view in this regard. Occasionally passage of the tube to the point of obstruction has required more time than expected, but we have not felt that this has been a deterring factor.

We recognized early the possible dangers of intubation of the small intestine in cases of strangulation. Obviously, strangulated obstruction requires early surgical intervention and even a few hours' delay may be costly. The problem here rests with the possibility of correctly diagnosing strangulated obstruction. That this can be done with some degree of accuracy is evident from the fact that, during the past year and a half, of twelve patients with strangulated obstruction who were treated in our service at City of Detroit Receiving Hospital all were operated on without delay.⁴ The errors in diagnosis were made in occasionally considering that nonstrangulated obstructions were strangulated.

Some comfort, in addition, was given to us by the statistics of McIver,⁵ which showed that in the type of case in which strangulation usually occurred (exclusive of external hernia, the diagnosis of which is usually obvious) the incidence was but 11 per cent. The conditions are volvulus, internal hernia and intussusception. Occlusion of a mesenteric artery or vein has a high mortality whether or not operation is performed, and we have come to feel that, with the possibility of better revascularization in a collapsed bowel, the patient's chances are a bit better if the intestine is kept decompressed. Since the incidence of true strangulation is low, the increase in total mortality should not be great even if the condition was not recognizable and operation was therefore delayed.

Support for the point of view which permitted us to proceed with this problem has been afforded in the cases we are now prepared to report. It is true that the number of patients with intestinal obstruction

3. Wangensteen, O. H., and Paine, J. R.: *Treatment of Acute Intestinal Obstruction with Suction by the Duodenal Tube*, *J. A. M. A.* 101:1532-1539 (Nov. 11) 1933.

4. Winfield, J. M., and Hartzell, J. B.: To be published.

5. McIver, Monroe A.: *Acute Intestinal Obstruction*, *Arch. Surg.* 25:1098-1134 (Dec.) 1932.

treated by intestinal intubation has been small and the experience therefore not truly conclusive. However, the series is large enough and the result striking enough to determine that the method is not likely to cause an increase in the death rate. The results rather indicate that a definite decrease in mortality should result.

The method of intestinal intubation has been described adequately elsewhere.⁶ It consists of the passage through the nose of a 16 to 18 gage tube from 10 to 12 feet in length on the end of which is attached

of the balloon. Failure to decompress ahead of the balloon will result in stoppage of the forward progress of the tube.

The cases which we are reporting are cases of acute intestinal obstruction or cases in which paralytic ileus associated with other conditions threatened the life of the patient. In addition, we have used intubation prophylactically in a large number of cases in which ileus was expected to result as well as in cases in which distention was of minor consequence in relation to a

Fatal Cases

Patient	Cause of Death	Decompression	Comment
Patients Who Died as a Result of Their Obstruction			
L. V., aged 51	Richter's hernia, perforation of ileum, peritonitis	Unsuccessful	Patient had diaphragmatic hernia, unrecognized Richter's hernia; tube never entered abdominal portion of stomach
M. T., aged 69	Perforation of ileum, peritonitis	1. Successful 2. Unsuccessful	Patient emaciated; obstruction at terminal ileum completely decompressed; patient died and appeared ready for operation after 26 days of intubation; operation deferred to allow gain in strength; after 4 days, obstruction reappeared and intestine perforated before tube could be passed; fine adhesive band found across terminal ileum, with pinpoint perforation
C. M., aged 51	Ileus involving entire gastrointestinal tract	Unsuccessful	Seen 6 hours before death; symptoms of 1 week's duration; 4 liters of fluid with much gas removed from stomach; intravenous injection of fluids started but patient died suddenly before second thousand cubic centimeters was introduced
N. G., aged 75	Intestinal obstruction	Successful (late)	Refused all treatment; home on release; returned 5 days later; wanted to die and refused intubation; successful intubation done when patient was moribund
H. B., aged 20	Intestinal obstruction	Successful	Refused intubation; operation, and adhesive band released; in good shape for 8 days; emphysema pulvis recurred and relieved by intubation; sudden return of abdominal pain 12 hours before death; x-ray examination showed complete decompression; autopsy refused
Patients Who Died from Causes Other Than Obstruction, with Distention Playing a Part in the Outcome			
J. W., aged 33	Septicemia following gunshot wound, right arm, pericarditis, empyema, peritonitis, multiple localized abscesses	Unsuccessful	Impossible to turn on right side; tube would not enter duodenum; enterostomy performed
J. O., aged 52	Nephritis, diabetes mellitus, uremia	Unsuccessful	Patient had old fistula following enterostomy; tube thought not to offer much advantage, inserted but irrational patient removed it; blood sugar 390, urea 115, carbon dioxide 33; chlorides always within normal limits
A. O., aged 77	Pyelonephritis, retroperitoneal abscess	Successful	Ten days' distention and obstipation; gastric suction 3 days before patient was seen by us; patient died of infection, but long continued distention probably played a part in her death
R. J., aged 26	Pyelonephritis, uremia	Successful	Patient's obstruction overcome at this and two previous admissions; previous admission for pyelonephritis; abdomen flat one week before death; chlorides within normal limits; blood urea 118
Patients Who Died from Causes Other Than Obstruction, with Distention Playing No part in the Outcome			
J. M., aged 48	Chronic granuloma of the retroperitoneal tissue and mesenteric lymph glands, evisceration, cachexia	Successful	Long tube used to keep distention down after evisceration
E. R., aged 39	Cardiovascular renal disease, lobar pneumonia	Successful	Distention completely relieved; tube out 1 week before death without return of troublesome distention
R. Z., aged 44	Encephalomalacia of left temporal lobe, cirrhosis of liver, chronic alcoholism	Successful	Ascites massive; intestine kept decompressed with tube
A. D., aged 60	Bronchopneumonia	Successful	Distention of small bowel controlled with long tube; large bowel controlled partially with enemas
R. L., aged 44	Ruptured appendix, subhepatic abscess, retroperitoneal cellulitis (right side)	Successful	Intestine kept successfully decompressed; patient died of infection

an inflatable balloon. When the tube is well into the duodenum the balloon is partially inflated, and peristalsis pulls the tube and balloon past the ligament of Treitz. At this point the balloon is fully inflated, to a capacity of from 40 to 60 cc., so that the intestine can act on a larger volume. The reason for not inflating the balloon fully in the duodenum is twofold: (1) If inflated fully the balloon and tip occasionally pull back into the stomach and (2) if too fully inflated the balloon passes with difficulty past the fixed portion of the upper part of the intestine, the lower part of the duodenum. As the tube progresses down the intestinal tract, fluid and gas are aspirated from the dilated intestine ahead

lethal outcome. These two types of cases we will not consider in this report, nor do our statistics include cases in which intubation was not used but operation was performed because of strangulation or suspected strangulation, unless alarming distention necessitated postoperative intubation.

Of the fifty-four patients, fourteen died. Of these, five died as a direct result of obstruction. The remaining nine patients died of other causes, and as a rule intubation was carried out to control distention associated with the conditions which caused death. In four cases distention appeared to be an associated factor in causing the death, and in five it was difficult to ascribe to the distention any part in the patient's death. The accompanying table contains the details of the fourteen fatal cases.

6. Miller, T. G., and Abbott, W. O.: *Am. J. M. Sc.* 187: 595-599 (May) 1934. Abbott, W. O., and Johnston, C. G.: *Surg., Gynec. & Obst.* 66: 691-697 (April) 1938. Johnston, C. G.: *J. Michigan M. Soc.* 37: 3 (July) 1938.

COMMENT

Intestinal intubation as an adjunct to the treatment of intestinal obstruction has proved successful in our hands in a small series of cases. That alone it cannot be depended on is obvious from the fact that intestinal obstruction is protean in its manifestations and causes. Each case must be individualized and the obstruction treated as to its specific requirements. Intubation does not exclude operative means of handling obstruction but rather facilitates any operative procedure which may be necessary.

The advantages of the method in properly selected cases are as follows:

1. It carries the patient past the period when operation is most dangerous.
2. It prepares the patient for operation by control of distention, thus making operation less traumatic for the patient and easier for the surgeon.
3. It affords a means of localizing the site of obstruction and frequently indicates its nature.
4. It permits oral feeding of the patient during a period when food and fluid are so essential and frequently has permitted us to improve the patient's nutritional state during the period of treatment.
5. It releases the tension above the site of obstruction and frequently reestablishes the normal passage of intestinal contents, thus permitting the patient to be operated on in the interval stage if advisable.
6. In the treatment of paralytic ileus this is the only method we know of which can uniformly be depended on to relieve the distention of the small bowel, which is not uncommonly fatal.

The disadvantages of the method are as follows:

1. It necessitates careful selection and evaluation of cases. It is not suitable for treatment of strangulated types of obstruction.
2. It requires hard work on the part of the surgeon and his associates. Passage of the tube and attention to details with regard to the patient and the equipment require continued attention.
3. It is not suitable for obstruction of the large bowel, since, despite the fact that the tube frequently traverses the entire intestinal tract, it cannot be depended on to reach the large bowel quickly enough to be of value.

In our series of fifty-four patients treated by intubation of the small intestine, fourteen patients died, a mortality of 25.6 per cent. Of these, five, or 9.3 per cent, died as a result of intestinal obstruction. In the remaining nine who died, intestinal intubation was carried out to relieve distention associated with other conditions which caused the death. In a larger series of cases we have intubated the small intestine for relief of distention or to prevent the development of distention, but we have not included these cases in our series. Our reason for excluding them is that the distention was not severe enough to have caused death or, in cases in which intubation was prophylactic, that we could not be certain that severe distention would have resulted without the tube.

This series does not include cases in which treatment was solely by operative means. The number of cases presented is small, and conclusions regarding mortality are difficult. The data do, however, indicate that intubation of the small intestine in selected cases has a definite place in the care of patients suffering from intestinal obstruction.

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ABSTRACT OF DISCUSSION

DR. DWIGHT L. WILBUR, San Francisco: The double and multilumen tube has proved to be of great value in the study of the physiology of the small intestine. It has given more information with regard to the function of the small intestine than has any other instrument. Because of the ease with which it may usually be passed into the small intestine it is natural that its use should have been extended from physiologic studies to those of diagnosis and treatment of diseases of the small intestine. Since decompression of a hollow viscus above an area of obstruction is one of the cardinal principles of surgical treatment of such diseases, the double lumen tube should be of great value in the treatment of intestinal obstruction. Dr. Penberthy and his associates have demonstrated that this is the case. There are dangers in the use of this method of treatment, as the authors have pointed out, and I should like to emphasize two of them. The first is that when suction is applied and the intestinal contents are drained for any period the situation is comparable to that in which an enterostomy opening is present. Under such circumstances considerable care must be exercised to maintain an adequate balance of fluid and chloride. It is probably not wise to maintain constant suction over too long a period. There is danger also in the treatment of patients who have strangulation of the small bowel, and the possibility that strangulation exists will probably constitute the greatest limitation of this particular method of treatment of intestinal obstruction. The principal therapeutic uses of the tube probably will be in the treatment of obstruction of the small intestine which is mechanical in nature, in the treatment of paralytic ileus and in the preoperative treatment of patients with obstruction who have marked abdominal distention. I think it will be wise for those who have not had much experience with this method of treatment to be prepared to operate in the first cases in which it is used or until such time as familiarity with its technic and with its possible limitations has been developed.

DR. FREDERICK A. COLLIER, Ann Arbor, Mich: About eight years ago, in the surgical section at the annual session, in a symposium on the treatment of intestinal obstruction, a young man read a paper on some experimental work on dogs. The discussion was led by the late great surgeon John B. Deaver, who said "Man is man and dog is dog, and never the twain shall meet." The poor laboratory worker passed out of the picture. There have been two notable contributions to the treatment of obstruction since that time, and both have come from the laboratory. Decompression as developed by Dr. Wangenstein and carried on by Dr. Johnston and Dr. Abbott is the greatest single technical contribution to abdominal surgery of the last decade. The second great contribution, given first by Dr. Hartwell and later by Dr. Hayden and Dr. Orr and other workers, showed the chemical changes brought on by vomiting in patients with obstruction. It is known that such patients may die from dehydration and from hypochloremia long before their lesion has passed beyond the control of the surgeon. During this year in the University Hospital my associates and I have interested ourselves in studying the question of salt loss and have found that hypochloremia is a real clinical entity that may kill. The normal value for plasma chlorides is about 560. If it falls below 500 symptoms begin to appear, and if it falls to the neighborhood of 300 the patient may die. One can suspect the presence of hypochloremia if the patient has been losing fluids from the gastrointestinal tract. The proof lies in the chemical determination of the plasma chlorides. There are, however, certain symptoms that suggest an imbalance of the chlorides; that is, in a patient who is not vomiting there will be loss of appetite, anorexia and later vomiting. The patient becomes depressed and confused mentally and may pass into coma. There is also a low pulse pressure. There are two situations to meet. When the patient has a normal value for chlorides when treatment is started and there are losses of fluid from the gastrointestinal tract due to enterostomy, fistula or duodenal suction, a volume-for-volume rule should be followed; that is, the substances drawn from the upper part of the gastrointestinal tract should be replaced liter for liter with physiologic solution of sodium chloride or Ringer's solution. The patient will then remain in chloride balance. On the other

hand, if the patient has been vomiting three or four days and the value for plasma chlorides is down, a rather simple formula may be followed which will replace the lost chlorides with a good deal of accuracy. Half a gram of salt per kilogram of body weight for each hundred points which the value for plasma chlorides is to be raised, given in the form of physiologic solution of sodium chloride, will bring the plasma chlorides to normal with accuracy. I wish to emphasize that many patients die of loss of chlorides as well as of dehydration. If one replaces the chlorides that have been lost, it should be remembered that they are always lost as hypotonic solutions, and one should use at least a physiologic solution of sodium chloride in replacing such fluids.

DR. CHARLES G. JOHNSTON, Detroit: We attempted in all these cases to follow the chloride level as well as to see that the patient had a definite fluid balance. I am happy that Dr. Collier brought out this point, because it is exceedingly important and was not discussed because of lack of time.

THE ETIOLOGY OF NAUSEA AND VOMITING OF PREGNANCY

PRELIMINARY REPORT

J. WILLIAM FINCH, M.D.

HOBART, OKLA.

This paper is a preliminary report on work being done to prove that nausea and vomiting accompanying pregnancy are due to an allergic reaction of the patient to the secretion of her own corpus luteum graviditatis.

This symptom complex is one which has been confronting the medical profession for centuries, the first record being made by Soranus of Ephesus¹ in the year 20 A. D.

Various authors² state that in from one half to two thirds of all obstetric cases there is nausea and vomiting to some degree during the first few months of pregnancy. So numerous have been the theories as to the etiology of this symptom complex³ that in this brief report no effort to discuss them will be made. The treatments recommended⁴ have been as variable and numerous as the theories of etiology.

The patient exhibiting nausea and vomiting may have these symptoms as a first indication of an existing pregnancy. The symptoms almost invariably begin between the third and the sixth week of pregnancy and gradually subside sometime near the fourth month of pregnancy.⁴ The symptoms may vary in severity from the mild case, so frequently seen, in which there is morning sickness with or without vomiting, to the moderate case in which there is nausea all day long, frequently vomiting, and extreme discomfort for weeks. Or the case may advance to the true hyperemesis gravidarum with a truly serious prognosis.

Hirst⁵ was the first to connect the nausea and vomiting of pregnancy with the functioning of the corpus luteum. He states that every woman during her menstrual life is constantly absorbing corpus luteum substance but that with the onset of pregnancy this absorption ceases. On this theory he administered

corpus luteum extract to a number of patients with surprisingly good results in alleviating or stopping their symptoms.

The corpus luteum, with impregnation, continues to develop instead of taking on the customary retrogressive changes during and after menstruation. The corpus luteum of pregnancy develops to a size much larger than the false corpus luteum; the colloid is more abundant in the organ and the granulosa cells are larger than before pregnancy.⁶ This enlargement takes place at the same time that symptoms of nausea and vomiting develop and the patient begins to be relieved of her symptoms about the fourth month, at which time retrogressive changes are taking place in the corpus luteum.

Considering that the development of the nausea and vomiting and the development of the corpus luteum of pregnancy occur at the same time and that the time of disappearance of the symptoms coincides with the time of retrogressive changes in the gland, I decided to conduct a series of tests on the theory that the nauseated and vomiting patient is allergic to her own hormone, develops her symptoms as a result of her sensitivity and returns to normal after the gland ceases to feed its secretion into her body in such quantity. On the same theory it can be assumed that Hirst was able to relieve his patients not by giving them a secretion in which they were deficient, as he assumed, but by desensitizing them and relieving them of their allergic reaction to the hormone.

Patients were tested by cleansing the skin with alcohol and injecting intradermally from 0.02 to 0.03 cc. of progestin in sterile cottonseed oil and recording reactions fifteen and thirty minutes later. Reactions were calibrated from negative to 4 plus, according to the size of the wheal and the surrounding erythema produced just as in intradermal injections of any food, drug or pollen extract or animal dander to determine a patient's degree of sensitivity. A control injection was made with sterile cottonseed oil in the same arm. The majority of the tests were made on the volar aspect of the forearm. A few patients were tested with a solution of progestin in sterile almond oil but the cutaneous reactions to the almond oil were so much greater than those to the cottonseed oil that the latter product was used in the remainder of the cases. One interesting notation has been that several of the pregnant patients who were nauseated and gave 3 or 4 plus reactions to the progestin intradermally have complained as late as five or six weeks after the intradermal injection that when they become nauseated severely the area of injection again becomes irritated and forms a wheal with a surrounding erythema and an itching sensation. I know of no way to explain this other than that the solution injected, being an oily one, is absorbed very slowly, and part of it remains in the skin for a protracted time. An extremely high percentage of the patients with nausea and vomiting of pregnancy gave a family history of allergy, as is noted in the reports of cases which follow:

REPORT OF CASES

CASE 1.—A secundipara, aged 27, who was nauseated with both former pregnancies, was very nauseated with the present pregnancy, vomited frequently. Nausea with each pregnancy began about the sixth week of gestation and lasted through the fifth month. Intradermal progestin gave a 4 plus reaction. The patient, her father, maternal grandmother and two brothers have seasonal hay fever and two sisters have asthma.

6. Novak, Emil: *Cyclical Changes in the Ovary*, in *Curtis Obstetrics and Gynecology*, Chapter VIII.

1. De Lee, J. B.: *Principles and Practice of Obstetrics*, ed. 5, Philadelphia, W. B. Saunders Company, 1928, pt. 2, chap. 28, p. 368.
2. De Lee, J. B.: *Principles and Practice of Obstetrics*, pp. 370-373.
3. Stander, H. J.: *Toxemias of Pregnancy*, in Davis, C. H.: *Gynecology and Obstetrics*, Hagerstown, Md., W. F. Prior Company, 1935, vol. 1, chapter 8, pp. 8 to 10. Mussey, R. D., and Randall, L. M.: *Toxemias of Pregnancy*, in *Obstetrics and Gynecology*, A. H. Curtis, ed., Philadelphia, W. B. Saunders Company, 1933, vol. 1, chapter XXX, pp. 1006-1008.
4. Stander, H. J.: *Toxemias of Pregnancy*, pp. 11-13.
5. De Lee, J. B.: *Principles and Practice of Obstetrics*, Chapter XXVII, pp. 368-369.
6. Hirst, B. C.: *A Textbook of Obstetrics*, ed. 8, Philadelphia, W. B. Saunders Company, 1918.

CASE 2.—A tertipara, aged 28, was moderately nauseated with her first three pregnancies. In this pregnancy nausea began about the fourth week and stopped at about four and one-half months. Nausea was moderate with no vomiting. Intradermal progestin gave a 2 plus reaction. The family history relative to allergy was not obtained.

CASE 3.—A secundipara, aged 31, was severely nauseated with her former pregnancies. In this pregnancy nausea began at about four weeks and was severe all day long with vomiting several times a week until about four and one-half months gestation. Intradermal progestin gave a 3 plus reaction. A brother has hay fever.

CASE 4.—A primipara, aged 30, was severely nauseated with her first pregnancy and vomited occasionally. She was moderately nauseated with this pregnancy with occasional vomiting. Intradermal progestin gave a 2 plus reaction. Nausea began at about one month gestation and ceased at about four months. The patient's parents died when she was an infant but she has one uncle with severe asthma.

CASE 5.—A secundigravida, aged 21, had one miscarriage at four months two years ago. She was mildly nauseated with that pregnancy. The cause of the miscarriage was unknown. The patient became extremely nauseated with this pregnancy at about one month gestation, vomiting almost all ingested food. Daily injection of extract of corpus luteum (each dose containing 0.02 Gm. of soluble extract) for twelve days resulted in complete cessation of vomiting, the patient having only transient periods of mild nausea after that time. Nausea completely disappeared at about four months gestation. Intradermal progestin gave a 3 plus reaction. There was no history of allergic diseases in the family.

CASE 6.—A tertigravida, aged 30, had one miscarriage at five months gestation three years ago, caused apparently by a long automobile trip. The patient has one child aged 19 months. She became nauseated with this pregnancy at about three weeks. She did not suspect pregnancy until nausea became intense with occasional vomiting. Intradermal progestin gave a 4 plus reaction. The patient's father has severe asthma. The patient is now receiving injections of progestin in oil, beginning with one-fourth international unit and gradually increasing at three day intervals to 2 international units. After three doses nausea was improved, and after five doses it had almost disappeared except for transient morning sickness.

CASE 7.—A woman, aged 26, miscarried twins at four months gestation six years ago following a large dose of an oxytocic drug self administered. She was greatly nauseated with frequent vomiting with that pregnancy. The present pregnancy was desired but the patient became intensely nauseated with frequent vomiting at about six weeks gestation. Nausea and vomiting ceased at about four and one-half months gestation. The patient's brother has seasonal hay fever and a nephew has asthma. Intradermal progestin six months before the patient became pregnant gave a 4 plus reaction. Intradermal progestin when the patient was at the end of the first trimester of pregnancy also gave a 4 plus reaction.

CASE 8.—A primigravida, aged 37, had tried for fifteen years to become pregnant without success. She became pregnant after the administration for three months of gonadotropic substance. She became extremely nauseated without vomiting at four weeks gestation, the symptoms increasing somewhat in severity until about the end of the first trimester and gradually diminishing during the fourth month of pregnancy. Intradermal progestin gave a 3 plus reaction. The patient's brother has severe migraine, as has also the patient.

CASE 9.—A primipara, aged 30, was not nauseated with her first pregnancy. With this pregnancy intense nausea with occasional vomiting began at about the third week of pregnancy. Nausea stopped at about the end of the fourth month. The patient's father has severe seasonal hay fever. Intradermal progestin gave a 4 plus reaction.

CASE 10.—A tertigravida, aged 21, became severely nauseated at about six weeks with her first pregnancy and had occasional attacks of vomiting. The symptoms subsided at about four

months gestation. The baby died at birth, apparently from poor obstetric care. With her second pregnancy she became nauseated at about six weeks and was nauseated severely with frequent vomiting until at three months she miscarried. With the last pregnancy the patient became nauseated at about six weeks gestation with about one vomiting spell a day. Nausea stopped at the end of the fourth month. The patient was delivered of a normal male infant at term. The patient's mother has asthma. Intradermal progestin gave a 2-plus reaction.

CASE 11.—A primigravida, aged 26, was extremely nauseated all day long with occasional vomiting from about six weeks until six months gestation. Repeated intradermal injections of extract of corpus luteum during the patient's period of nausea all gave a 4 plus reaction. The patient also has severe seasonal hay fever and has frequently suffered nausea with the first day or two of the menses. The patient was delivered of a normal male at term. Nine months after delivery an intradermal injection of progestin in oil gave a 3 plus reaction.

CASE 12.—A primigravida, aged 21, now about seven weeks pregnant, has nausea which began at about four weeks gestation; she is now nauseated all day long without vomiting. The odor of food nauseates her severely. The menses have always been every twenty-five days and of eight days' duration. The patient's maternal uncle has asthma. Intradermal progestin gave a 2 plus reaction.

CASE 13.—A primigravida, aged 24, is now about ten weeks pregnant. Nausea began at about three and one-half weeks gestation before the patient suspected pregnancy. At six weeks the nausea was intense with vomiting of practically all ingested food. At this time treatment was begun, 1 cc. of extract of corpus luteum (containing 0.02 Gm. of soluble extract) being given at forty-eight hour intervals for three doses, then one-half international unit of progestin in oil at the same interval for three doses, then 1 international unit, 1½ and 2 international units respectively at each of the next three doses. After the fourth dose the symptoms were markedly alleviated and at this writing the patient, having had the foregoing treatment, now has no vomiting and only transient attacks of mild nausea. The patient's father and sister both have severe seasonal hay fever. Intradermal progestin gave a 4 plus reaction.

CASE 14.—A woman, aged 29, who has one child aged 18 months, was nauseated slightly for about six weeks during the early part of that pregnancy but did not vomit. There was no history of allergy in the family. Intradermal progestin gave a 2 plus reaction.

CASES 15 to 20 inclusive.—The patients' ages ranged from 19 to 27 years; four are primigravidas and one is a primipara. In each case there was an extremely slight amount of nausea and no vomiting following about five or six weeks of gestation. The duration of the symptoms varied from five days to two weeks. There was no history of allergy in the families of any of these patients. Intradermal progestin gave a 1 plus reaction in all five cases.

CASES 21 to 24 inclusive.—The patients' ages ranged from 21 to 33 years; two are primigravidas, one is a primipara and one is a quintipara. None of these patients have had even the slightest degree of nausea or vomiting with the present or any previous pregnancy. There was no history of allergy in the families of any of these four patients. Intradermal progestin gave negative reaction in all cases.

CASE 25.—A virgin, aged 20, has seasonal hay fever. Her father has seasonal hay fever. The patient has had no nausea with the menses. Intradermal progestin gave a 1 plus reaction.

CASE 26.—A virgin, aged 20, with no history of allergy in her family, has had no nausea with the menses. Intradermal progestin gave a 1 plus reaction.

CASE 27.—A virgin, aged 21, with no history of allergy in her family, has had no nausea with the menses. Intradermal progestin gave a 1 plus reaction.

CASE 28.—A woman, aged 52, had a surgical menopause fourteen years ago. She has one child, now aged 30. With that pregnancy the patient had a very mild morning sickness. She had a normal menstrual history up to the age of 35 or 36, at

which time she had an operation for a fibroid uterus and ovarian cysts. There was no history of allergy in the family. Intradermal progestin gave a 1 plus reaction.

CASE 29.—A virgin, aged 15, whose menses began at 11 years and pubic hair developed at 9, had marked breast development at 10½. At 13 she began having extremely heavy periods and at 14 she had a curettage to stop a prolonged menstrual period. Curettings were of hyperplastic endometrium. Following this curettage the patient was normal for ten months, with the exception of two menses which lasted nine and twelve days respectively. At 15 the patient was seen with a heavy menstrual flow, which had existed for three weeks before she consulted a physician. Large doses of progestin checked the flow but curettage of the hyperplastic endometrium was necessary to stop it. The condition is now progressing normally with the administration of corpus luteum during the week before the expected menstrual period and with small doses of thyroid extract during the entire cycle. The symptoms are probably a result of oversecretion of estrogen from persistence of the graafian follicle, and, because of a probable lack of a normal amount of progestin throughout most of her sexual life, she should theoretically at least be nonsensitive to progestin. There is no history of allergy in the family. Intradermal progestin gave a negative reaction.

CASE 30.—An octipara, aged 44, was nauseated severely and vomited in moderate degree with all eight of her pregnancies. Her present complaint is eczema due to food allergy. The patient also has seasonal hay fever. Intradermal progestin gave a 3 plus reaction.

COMMENT

The menstrual history and progress in all the cases was negative unless otherwise stated in the reports.

This is only a preliminary report, but I believe that the uniformity of the results of the intradermal tests, the good results on the patients treated along the lines of allergic desensitization and the huge number of women afflicted with these symptoms at all times merits an investigation on a large scale. It would also be of interest to test with intradermal progestin a series of young girls before puberty.

I believe that patients presenting nausea and vomiting either have inherited directly a sensitivity to progestin or, more probably, have inherited the allergic tendency and become sensitive to their own corpus luteum secretion during their menstrual cycles or from the corpus luteum of a previous pregnancy.

If further investigation confirms these observations, one might well assume that a patient desiring pregnancy could be tested for sensitivity to progestin and, if found sensitive, could be desensitized before impregnation or before the corpus luteum of pregnancy reaches the stage of enlargement necessary to produce the symptoms of nausea and vomiting. This treatment would consist of graduated doses of progestin injected at closely spaced intervals until the patient is desensitized and the symptoms either do not develop or are relieved if they have already developed. It would be of further benefit, I believe, if a solvent other than oil could be used for the progestin, since the various oils now in use are more or less irritating to the skin of patients when injected intradermally and are slowly absorbed. A solution less irritating and more quickly absorbed would probably also enhance the treatment of nausea and vomiting along these lines by allowing intradermal injections to be given concurrently with the subcutaneous injections for desensitization.

SUMMARY

1. Nausea and vomiting of pregnancy develop at the same time at which the corpus luteum of pregnancy

reaches an appreciable size. The symptoms disappear at about the time the gland is known to begin retrogressive changes.

2. In a series of patients with nausea and vomiting of pregnancy in varying degrees when injected intradermally with from 0.02 to 0.03 cc. of progestin in oil a cutaneous reaction developed directly proportional to the severity of the symptoms.

3. A control series of patients who were not nauseated and in the pregnant state gave negative cutaneous reactions when tested in the same manner.

4. Patients treated with subcutaneous corpus luteum extract and progestin along the lines of allergic desensitization were gradually relieved of their symptoms.

5. A high percentage of the patients with nausea and vomiting of pregnancy either had other diseases of allergy or gave a family history of allergy.

CONCLUSIONS

1. The nausea and vomiting accompanying pregnancy is due to an allergic sensitivity of the patient to the secretion of her own corpus luteum of pregnancy.

2. Desensitization may be accomplished by injection of graduated doses of progestin, thus alleviating or stopping the patient's symptoms.

3. Intradermal testing may determine, even before pregnancy, whether a patient will or will not be nauseated when pregnant by determining whether or not she is sensitive to progestin.

Oklahoman Building.

SENSITIVITY TO RABBIT SERUM

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AND

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The purpose of this study was to determine whether rabbit serum can produce reactions of the skin and the eye that are significant.

The advantages of rabbit antipneumococcus serum have been well summarized by Horsfall and his co-workers.¹

In the first paper on the clinical use of rabbit serum, these authors² reported its administration in twenty-two cases of pneumonia and stressed the fact that the intradermal reactions to rabbit serum were not significant as an indication of sensitivity. Neither conjunctival nor intravenous tests were positive in this series of cases.

In the second paper, they³ reported on the use of rabbit serum in sixty-seven cases of pneumonia. They reiterated that no reliance had been placed on the results of intradermal tests because of the commonness of false positive reactions. A marked positive intradermal reaction occasionally occurs in persons subsequently shown not to be sensitive to rabbit serum on intravenous injection. These authors also stated that the conjunctival test has been of little aid in the judging of sensitivity, though a positive reaction should be regarded as an

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1. Horsfall, F. L., Jr.; Goodner, Kenneth, and MacLeod, C. M. *Science* 84:579 (Dec. 25) 1936.

2. Horsfall, F. L., Jr.; Goodner, Kenneth; MacLeod, C. M. and Harris, A. H.: Antipneumococcus Rabbit Serum as a Therapeutic Agent in Lobar Pneumonia, *J. A. M. A.* 108: 1483 (May 1) 1937.

3. Horsfall, F. L., Jr.; Goodner, Kenneth, and MacLeod, C. M.: *New York State J. Med.* 38: 245 (Feb. 5) 1938.

indication that all subsequent procedures should be undertaken with the greatest caution. They expressed satisfaction with the intravenous test, though two of the sixty-seven patients reacted positively to it.

The conjunctival test has been relied on as a guide in the use of antipneumococcus horse serum. We should expect rabbit serum to follow the same rule.

To determine whether it does, we performed intradermal and conjunctival tests on 101 patients. Since allergic persons are more apt to give reactions, we chose to carry out the work with the allergic patients in the clinics of the Bellevue Hospital and the New York University College of Medicine.

Intradermal and conjunctival tests with normal rabbit serum diluted 1:10 and containing 0.5 per cent chlorobutanol were performed on 101 patients. The conjunctival test was done by instilling 1 drop of serum into the lower conjunctival sac of the right eye. The intradermal test consisted of the raising of a $\frac{1}{8}$ inch (0.32 cm.) wheal in the skin of the arm by an injection of from 0.02 to 0.01 cc. Because every patient had one or more negative intradermal reactions, controls of diluting fluid were used only when it was necessary to differentiate a dermatographic skin. The reactions were read in from ten to fifteen minutes, as follows:

0—no reaction

1 plus—erythematous flare and/or slight wheal

2 plus—definite wheal from 1 to 2 cm. in diameter

3 plus—wheal from 1 to 2 cm. in diameter with no/or slight pseudopodia

4 plus—wheal 2 cm. in diameter or larger, with marked pseudopodia

Conjunctival tests were regarded as positive or negative.

This series of 101 patients contained fifty-four males and forty-seven females, with the age ranging from 11 to 79 years.

The tests with rabbit serum gave sixty-nine negative intradermal reactions, twenty-two flare reactions, six 2 plus reactions, two 3 plus reactions and two 4 plus reactions. Only one person gave a positive conjunctival reaction in addition to the 4 plus intradermal reaction. This patient gave an immediate positive intradermal and conjunctival reaction, followed within five minutes by a systemic reaction, with urticaria, angioneurotic edema and asthma, requiring repeated injections of epinephrine for relief. These symptoms persisted in a mild way for several days, requiring the continued use of ephedrine, augmented by occasional administration of epinephrine.

We feel that the intravenous injection of rabbit serum in this case might have been fatal.

SUMMARY

Intradermal and conjunctival tests with rabbit serum were performed on 101 allergic patients. One person gave a systemic reaction to the conjunctival test, and the increasing use of rabbit serum prompts us to urge caution in the administration of this agent.

The conjunctival reaction, we feel, is a good indicator of general sensitivity, and while fewer persons may be sensitive to rabbit serum than are sensitive to horse serum, nevertheless we feel that the same care should be used with rabbit as with horse serum.

39 West Fifty-Fifth Street.

SULFANILAMIDE TREATMENT OF TRACHOMA

PRELIMINARY REPORT

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ROSEBUD, S. D.

In August 1937 my associates and I began to use sulfanilamide in the treatment of trachoma at the Rosebud Indian Hospital. For the experiment we selected two patients whose condition had been diagnosed as trachoma by an eye specialist in the Indian Service and by several other physicians in the Indian Service who are especially experienced with trachoma. One of the two patients had had trachoma for two years, the other for eighteen months. Both patients had had grattage, followed by treatments with silver nitrate given intermittently during the period of their infection, with no noticeable improvement. On the basis of their body weight they were given one-third grain (0.02 Gm.) of sulfanilamide, with an equal amount of sodium bicarbonate, a pound daily for ten days. Then the dose was decreased to one-fourth grain (0.016 Gm.) of sulfanilamide a pound daily for fourteen days. No other medication was allowed during this period. Within five days after treatment was begun we were able to see changes in the conjunctiva; the redness gradually disappeared, the granules and papules decreased in size and the blood vessels became increasingly visible. With a maintenance dose of one-fourth grain of sulfanilamide a pound daily these two patients were apparently cured of trachoma within one month. To date neither has shown signs of recurrence.

On Jan. 6, 1938, we started sulfanilamide treatment with thirteen patients who had been under continuous treatment for trachoma for periods varying from one to seven years and who were picked for the purpose from a group of patients with trachoma. Three were dismissed on January 16, apparently cured; the remaining ten were found to be greatly improved after being under treatment for eight days and were treated for two weeks longer.

After using sulfanilamide in the aforementioned dose for the treatment of trachoma in 140 patients, we are able to summarize briefly the improvements noted:

1. Improvement of subjective symptoms:

(a) Cessation of lacrimation within twenty-four hours.

(b) Loss of photophobia within twenty-four hours.

(c) Improvement of vision within seventy-two hours in cases of pannus.

2. Improvement of objective symptoms:

(a) Paling of the conjunctiva.

(b) Paling of the trachomatous patches and flattening of the granules and follicles. At the end of three weeks of treatment a few flat-topped granules remained, and we found that only after several months did these entirely disappear. The medication was not continued during these several months, however. The ninety-three patients treated in boarding schools during January and discharged as improved are examined at monthly intervals and continue to show improvement in the conjunctiva without further medication and with no exacerbations of any kind. Examination May 12 showed twelve with slight activity.

(c) In the cases in which there had been no scarring from instrumentation, the conjunctiva at the end of two months apparently resumed its normal velvety texture.

Read before the Section on Ophthalmology at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 15, 1938.

(d) The blood vessels of the conjunctiva become more visible on the fifth or sixth day of treatment, and daily thereafter they become more normal.

(e) In thirty cases of pannus treated in the hospital we noted that the opacity began clearing between the eighth and the fifteenth day, depending on the density of the pannus, with great improvement of vision.

(f) The granules on the lower lids were found to be the last objective symptoms to disappear.

Our work with sulfanilamide in the treatment of trachoma has to date been done with 140 patients, all either hospitalized or under the close supervision of nurses in our three boarding schools. The reactions have been surprisingly few and mild. In three cases dermatitis developed. Three days after withdrawal of the sulfanilamide this cleared up, leaving no sequelae. Four patients complained of mild vertigo and headache. Withdrawal of the sulfanilamide for twenty-four hours cleared these symptoms, and the patients were able to resume treatment. We noted no elevation of temperature coincident with the administration of sulfanilamide.

Our experience with this method of treatment thus far has made us extremely sanguine. It is still too early to speak of the results as "a cure," for we do not know whether there will be recurrences or not. Moreover, not all patients respond alike, so that standardization of treatment is as yet impossible. Consequently, we offer our observations in the nature of a preliminary report, with the hope that this method of treatment will be used by others and in a number of cases sufficiently large to determine the exact value.

REPORT OF CASES

CASE 1.—H. R. B., a full-blooded Sioux, who was 52 years old, weighed 81.1 Kg. and had a negative Wassermann reaction, had suffered from chronic trachoma since April 1932 and had been hospitalized for treatment for a total of 104 days prior to admission Jan. 24, 1938. In March 1933 a grattage was done, which was only partly palliative, for it was followed in November 1933 by stretching of the conjunctiva and rubbing gauze over the roughened lids. Intermediate treatment consisted of irrigation with zinc and boric acid solutions alternated with instillations of 1 per cent silver nitrate. In spite of this rather persistent treatment, by October 1936 the conjunctiva of each lid was thickened, opaque and replaced by scars; pannus extended over the anterior surface of the cornea. There were numerous granular patches on the lids, no visible blood vessels in the lids, marked photophobia and dense pannus extending over the upper half of the cornea, and the patient was unable to read print, for his vision could not be corrected on account of the pannus. The vision of the left eye was 20/160 and of the right eye 20/40. February 7 the vision of both eyes was 20/30. February 8 the vision of the right eye was 20/30 and of the left eye 20/20. February 12 the vision was normal, the lids were clearing and numerous blood vessels were visible in the conjunctivas.

CASE 2.—V. L. W., of three-fourths Sioux blood, who was 47 years old, weighed 81.1 Kg. and had a negative Wassermann reaction, had suffered from trachoma since childhood. The family history revealed that both parents and three siblings had trachoma. The patient's mother was totally blind during the last decade of her life. Examination on admission Feb. 3, 1938, showed only light perception in the right eye. The patient could distinguish fingers with the left eye at a distance of 15 inches. The pupils were completely obscured because of corneal pannus. The patient complained of severe photophobia; intense lacrimation was present. February 4 the administration of sulfanilamide was started. By February 7 the patient could distinguish the correct number of fingers at 40 inches with the left eye. With the right eye he could see the examiner's hand at 36 inches. February 8 he could read the top line and

the first three letters of the second line on Sneller's chart at 10 inches. February 12 his reading ability remained the same. Some blood vessels were visible; the lids were less red; the pupils were visible to the examiner. The patient volunteered the information that his vision had improved to the extent that he was able to see more than ever before in his life. February 15 he read the first and second lines at 28 inches and he now has coarse vision, being able to see his way about the ward and to the bathroom. He says that his eyes are not painful and that there is no photophobia.

ABSTRACT OF DISCUSSION

DR. HARRY S. GRADLE, Chicago: Stimulated by the original report of Dr. Loe to the Department of the Interior on the effects of sulfanilamide in trachoma among the Indians, I started a series of cases in my own trachoma clinics with that drug. Twenty-five cases were selected among the patients in the Trachoma Clinics of Southern Illinois, where all are outpatients, and sixteen in the Illinois Eye and Ear Infirmary, all of whom remained in the hospital. Of this number, five were forced to discontinue the drug within a few days because of systemic symptoms that ranged from mere headache and nausea to actual cyanosis, necessitating digitalis. The cases in the infirmary hospital were followed from the laboratory standpoint daily with the following observations: (a) Bacteriologically, there were organisms found in only a few cases. (b) The hemoglobin showed a fairly uniform decrease of from 10 to 15 per cent. (c) The red blood count showed no change except for a moderate decrease in isolated cases. (d) The white blood count showed a fairly uniform decrease of from 1,000 to 3,000 cells. With regard to the impressions gained from three weeks' observation of these cases under sulfanilamide, without any local treatment except a cleansing wash with physiologic solution of sodium chloride, the following seemed to be the salient features: 1. Trachoma II and III responded fairly uniformly in a most surprising fashion in that the velvety patches and hypertrophies disappeared in short order. The thickened and hyperemic conjunctiva became thinner and pale, the individual vessels became visible, and the secretion disappeared in the majority of cases. The results of three weeks of sulfanilamide approximated those of from three to six months of local treatment, but without scar formation. 2. Regardless of the stage, photophobia and lacrimation disappeared in short order. This subjective improvement was most striking and, to the patients, most gratifying. 3. In trachoma IIB and IIIA and IIIB there was a marked improvement in vision in cases in which the vision was decreased because of pannus. In the older and more malignant cases and those in which there were corneal scars due to old ulcers, the visual improvement was negligible. But in some instances the visual results were almost miraculous. 4. In trachoma IV and in malignant cases of trachoma IIB, practically no improvement could be noted. It would appear that in the use of sulfanilamide we have a new means of combating the more acute stages of trachoma. The drug is not without danger and should be taken only when medical observation is possible every twenty-four to forty-eight hours.

University Tradition in America.—From the first foundations to the present, four main streams have watered the soil in which the universities have flourished. These ultimate sources of strength are, first, the cultivation of learning for its own sake; secondly, the general educational stream of the liberal arts; thirdly, the educational stream that makes possible the professions; and, lastly, the never-failing river of student life carrying all the power that comes from the gregarious impulses of human beings. All four streams are easily discerned bringing life to the English universities in the first half of the seventeenth century. For this reason Oxford and Cambridge flourished; and because they flourished, their sons who migrated to this strange land desired to cultivate the same sturdy tradition even in a wilderness.—James Bryant Conant in the Tercentenary of Harvard College, Cambridge, Mass., Harvard University Press, 1937.

Clinical Notes, Suggestions and New Instruments

PNEUMOCOCCUS TYPE VII MENINGITIS, TREATED WITH SULFANILAMIDE AND SPECIFIC SERUM, WITH RECOVERY

RICHARD Z. QUERY, M.D., DURHAM, N. C.

Pneumococcic meningitis has been considered an almost universally fatal disease, the mortality being about 95 per cent. Clinical observers have reported occasional cures by the use of type specific antipneumococcus serum or by the use of ethylhydrocupreine hydrochloride. These two therapeutic agents in combination have been used in a few additional cases, but the results are far from gratifying. Recoveries are so rare that they usually gain access to the medical literature.

Experimenters have demonstrated that sulfanilamide has a bacteriostatic and bacteriocidal action on pneumococci both in vivo and in vitro. Rosenthal¹ found that the drug was quite effective in peritonitis in the mouse caused by pneumococcus types I, II and III, results which were confirmed by Long and Bliss.² Cooper and Gross³ produced type III pneumonia in mice and noted that the mortality rate was decreased and the survival period prolonged in those which did succumb. In fact, these observers report that sulfanilamide is just as effective as the type specific pneumococcus serum and, further, that the combination of sulfanilamide and pneumococcus antiserum gave better results than either of these measures used individually. Heintzelman⁴ studied nine cases of type III lobar pneumonia treated with sulfanilamide in which there was a mortality rate of 22 per cent, whereas in ten similar cases in which symptomatic treatment was given the mortality rate was 74 per cent.

As to the efficacy of sulfanilamide in the treatment of other forms of purulent meningitis, excellent results are being reported. In some of the most hopeless cases of streptococcic and meningococcic meningitis remarkable cures have been effected. So far I have been able to find only two reports⁵ in the medical literature of the successful use of this new drug in cases of pneumococcic meningitis.

It is my purpose in this paper to report a case of type VII pneumococcus pneumonia and meningitis in which the combination of antiserum and sulfanilamide caused a dramatic cure.

REPORT OF CASE

History.—A Negro, aged 33, a worker in a tobacco factory, admitted to Duke Hospital Nov. 11, 1937, complained of pain in the right chest of two days' duration.

The family, marital and past histories were irrelevant.

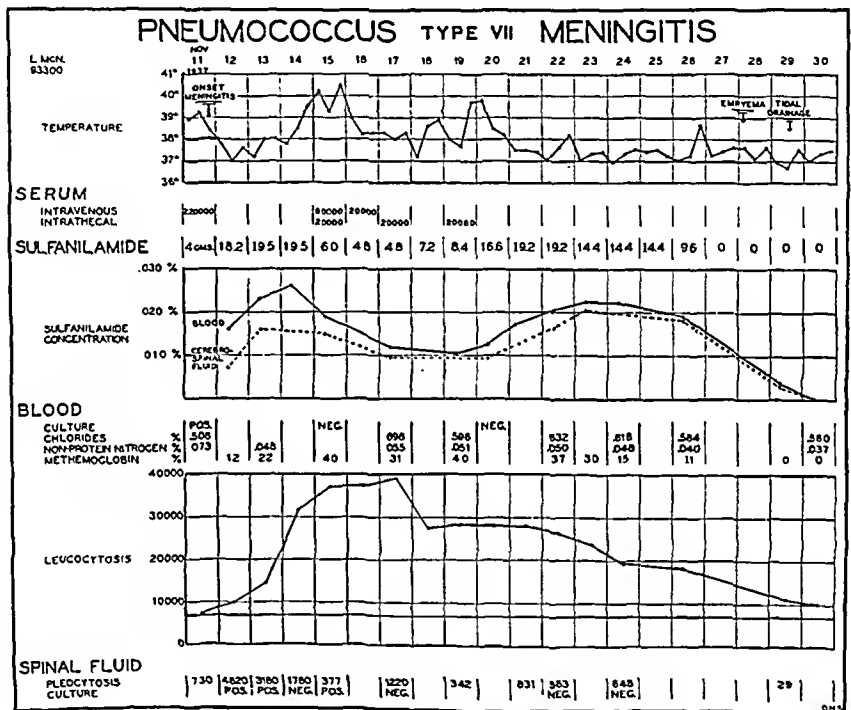
Eleven days before admission he contracted an infection in the upper part of the respiratory tract following exposure to cold, damp weather. Two days before admission he noticed the onset of generalized bodily aches, fever and sharp pains in the right anterior part of the chest during a deep inspiration. The cough,

which he had had from the beginning of his illness, became more productive and sputum was described as blood streaked. He did not have a chill. These symptoms increased in severity until admission.

Examination.—The temperature was 38 C. (100.4 F.), pulse rate 108, respiratory rate 30 and blood pressure 125 systolic, 88 diastolic. The patient was well developed, well nourished and obviously acutely ill. He was in slight respiratory distress but there was no cyanosis of the lips or nail beds. He coughed frequently, producing a moderate amount of blood-streaked sputum.

Expansion of the right side of the chest was limited. Tactile fremitus was increased over the right lower lobe posteriorly. The percussion note was dull over this area; the breath sounds were bronchovesicular; many fine rales were heard at the end of inspiration. The remainder of the general physical examination was negative.

Accessory laboratory examinations showed hemoglobin 14.2 Gm. (Sahli), red blood cells 4,750,000 and white blood cells 11,000, of which 95 per cent were polymorphonuclear neutrophils with a preponderance of young forms. The urine showed



Course in case of pneumococcus type VII meningitis.

1 plus albumin. The Wassermann and Kahn reactions of the blood were negative. A smear of the sputum showed many gram-positive encapsulated lancet-shaped diplococci. Typing of the sputum by the Neufeld method demonstrated type VII pneumococci. This was confirmed by mouse inoculation and retyping. A blood culture taken on admission was reported the following day as showing innumerable colonies of type VII pneumococci. A film was taken by a portable x-ray machine which showed diffuse clouding throughout the lower two thirds of the right lung and slight mottling extending out from the left hilus. The general appearance was that of bronchopneumonia.

One hour after admission type VII antipneumococcus serum was administered intravenously, and during the course of the next fourteen hours 220,000 units was given, with some improvement. Eighteen hours after admission the patient became drowsy and complained of severe headache. It was found at this time that his neck was stiff and Kernig's sign was positive. A lumbar puncture was done. The cerebrospinal fluid was under increased pressure and turbid. The Pandy test was positive. There were 730 cells, predominantly polymorphonuclear neutro-

From the Department of Medicine, Duke University School of Medicine.

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3. Cooper, F. B., and Gross, Paul: Proc. Soc. Exper. Biol. & Med. 36: 678 (June) 1937.

4. Heintzelman, J. H. L.; Hadley, P., and Mellon, R. R.: Am. J. M. Sc. 193: 759 (June) 1937.

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phils; the smear revealed many gram-positive encapsulated diplococci. The spinal fluid culture was positive for type VII pneumococci.

The patient was started on sulfanilamide by mouth, 4 Gm. being given on the first night, 18.2 Gm. the second day and 19.5 Gm. the third day. The concentration of sulfanilamide in the blood and spinal fluid reached 23 and 16 mg. per hundred cubic centimeters respectively. The methemoglobin was 40 per cent, as shown in the accompanying chart. On the fifth day he became completely maniacal and restraints were applied. It was impossible to give medication by mouth, so sulfanilamide was given by subcutaneous infusion in 1 per cent solution, with a corresponding decrease in the concentration of the drug in the blood and spinal fluid. Type VII antipneumococcus serum was again given intravenously and 60,000 units intrathecally. By the tenth day the mania had disappeared and he was able to take medication and nourishment by mouth, and the sulfanilamide dosage was increased. During this time he was showing rapid clinical improvement but was disoriented as to time and place. On cessation of the sulfanilamide his sensorium completely cleared.

On his seventeenth hospital day signs of fluid were demonstrated at the base of the right lung; 450 cc. of thick, greenish fluid was removed in which gram-positive diplococci were demonstrated. Culture of this fluid revealed type VII pneumococci. Tidal irrigation was instituted and an uneventful recovery ensued.

Follow Up.—The patient was seen five months after discharge from the hospital. He had gained weight and was feeling perfectly well. He had no headaches, convulsions or other residual effects that could be ascribed to the meningitis.

SULFANILAMIDE THERAPY FOR SUPPURATIVE PYLEPHLEBITIS AND LIVER ABSCESES

REUBEN OTTENBERG, M.D., AND MAURICE BERCK, M.D., NEW YORK

Suppurative pylephlebitis with multiple liver abscesses is an extremely grave disease. It most commonly follows acute appendicitis but also may complicate a great variety of intra-abdominal and rectal infections. The diagnosis may be difficult, and in many more cases the disease is recognized on the postmortem table rather than during life. The incidence of the condition has been appreciably smaller in recent times, owing to earlier operative intervention for acute appendicitis. In the older statistics necropsy reports of patients dead of acute appendicitis revealed pylephlebitis and liver abscesses in 4.7 per cent (Fitz),¹ 5 per cent (Armstrong)² and 5 per cent (Petren).³ More recent analyses showed 0.4 per cent (Gatch and Durman)⁴ and 0.3 per cent (Hawkes).⁵ Colp,⁶ in analyzing 2,841 cases of acute appendicitis, noted an incidence of 6.8 per cent of preoperative chills; in only a small fraction of these cases did the condition progress on to the septic course of pylephlebitis. He found that a single preoperative chill was of little prognostic importance. However, when pylephlebitis subsequently developed there was usually a preoperative history of multiple and protracted chills. In the case of early acute appendicitis in which there has been but a single chill there is usually locally contiguous phlebitis of the appendicular veins. Early operation succeeds because it eradicates the local phlebitis by removal of the appendicular mesenterium in the course of appendectomy.

From the Medical Service of Dr. B. S. Oppenheimer and the Surgical Service of Dr. Ralph Colp, Mount Sinai Hospital.

1. Fitz, R. M., cited by Hawkes.⁵
2. Armstrong, G. E.: Introduction to a Discussion on Appendicitis, Brit. M. J. 2: 945, 1897.

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In isolated instances spontaneous recovery has occurred when multiple liver abscesses were thought to be present.⁷ However, doubt must always exist as to the nature of a condition regarded as suppurative pylephlebitis when recovery has occurred without laparotomy and examination of the liver. In a few instances operative drainage of liver abscesses due to appendicitis has resulted in recovery.⁸ Cases in which appearances at necropsy were regarded as those of healed suppurative pylephlebitis have been recorded.⁹

Operative intervention to treat the condition by ligation of branches or the main trunk of the portal vein has been attempted in many instances. These procedures have consisted chiefly (1) of ligation of the ileocolic vein at the time of appendectomy¹⁰ if a history of chills and the operative evidence of progressive thrombosis of the contiguous venous radicles were present, and (2) of ligation of the ileocolic superior mesenteric or portal veins (Braun,¹⁰ Colp,⁶ Taylor) in those instances in which suppurative pylephlebitis occurred as a later complication. The results of operative intervention (except as a primary prophylactic operation for restricted thrombophlebitis in the appendical area)¹¹ have been most disappointing.

The general consensus is that suppurative pylephlebitis with multiple liver abscesses is almost invariably fatal.⁷ The prognosis with any form of therapy is considered uniformly bad.

The micro-organisms seen at autopsy are of intestinal origin—usually colon bacilli, streptococci or various anaerobes. Of these the colon bacilli at least are known to be susceptible to sulfanilamide therapy.¹² It was this fact that led us to try the drug in the present cases.

It is our purpose in this communication to report two cases—the first of probable, i.e., clinically diagnosed, pylephlebitis following incision of an infected thrombosed hemorrhoid; the second of postappendiceal suppurative pylephlebitis with multiple liver abscesses (proved by biopsy of the liver). In both cases sulfanilamide therapy was followed by recovery.

REPORT OF CASES

CASE 1.—O. N., a man, aged 23, with a clinical diagnosis of pylephlebitis following an operation on an infected hemorrhoid, was admitted Sept. 22, 1937, and discharged October 24. He complained of fever, chills and abdominal pain. Two weeks before admission an infected thrombosed hemorrhoid had been incised by his private physician. Local pain had persisted. Six days before admission he suddenly experienced a severe chill and a temperature of 103 F. He then experienced fever and one or two chills a day with abdominal pain. When first seen he was having a chill and his temperature was 104 F. On physical examination there were shock tenderness over the liver and rebound tenderness over the right costal margin. On rectal examination there was a healing sinus leading up to an area of induration and tenderness in the anterior wall. The blood count showed hemoglobin content 105 per cent, red cells 5,300,000, white cells 13,250, polymorphonuclear leukocytes 68 per cent (33 per cent segmented, 35 per cent staff) eosinophils 1 per cent, monocytes 1 per cent, lymphocytes 30 per cent. The administration of sulfanilamide was started immediately, 1 Gm. every four hours for the first three days, then 0.5 Gm.

7. Cited by Rolleston, H. D., and McNee, J. W.: Diseases of the Liver, Gall Bladder and Bile Ducts, ed. 3, New York, Macmillan Company, 1929, p. 120. Pylephlebitis Complicating Appendicitis, editorial, J. A. M. A. 110: 816 (March 12) 1938.

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11. Braun.¹⁰ Hawkes.⁵

12. Buttle, G. H. A.; Parrish, H. J.; McLeod, Morag, and Stephenson, Dora: Chemotherapy of Typhoid and Some Other Nonstreptococcal Infections in Mice, Lancet 1: 681 (March 20) 1937.

every four hours for the following two weeks and until his temperature had been normal for five days.

During the first two weeks of treatment he was very ill, with an irregular temperature ranging from 102 to 104 F. He showed a moderate grade of jaundice during the first week, the urine showing traces of bile and urobilinogen to a dilution of 1:250. The blood bilirubin was 1.6 mg. per hundred cubic centimeters and the direct van den Bergh test gave a negative reaction. The patient had only one chill after his admission to the hospital; this was accompanied by a temperature of 104 F. after one week of treatment. During the second week of treatment the temperature gradually fell to normal and remained normal thereafter. The tenderness over the liver and the jaundice disappeared and the patient proceeded to make a complete recovery.

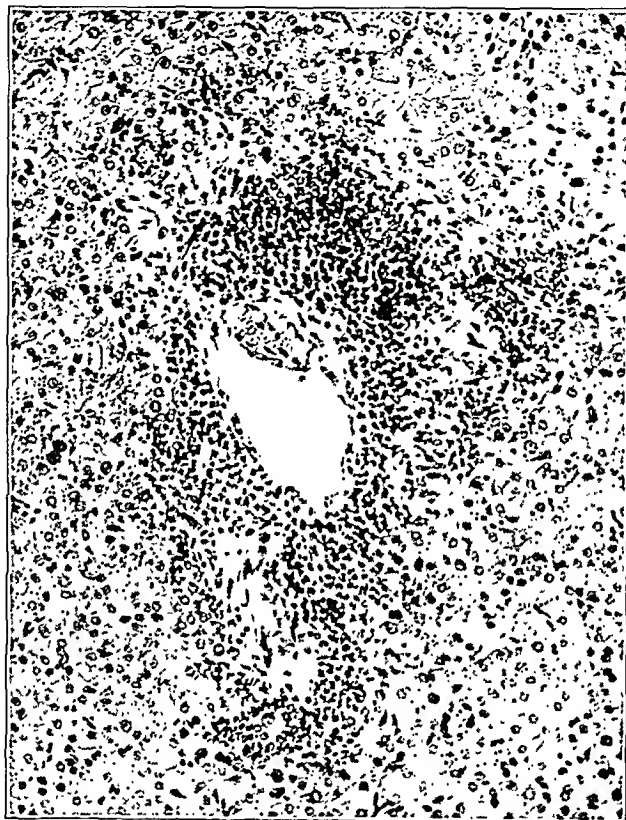
CASE 2.—T. C., a man, aged 40, a Puerto Rican with a clinical diagnosis of postappendical suppurative pylephlebitis with multiple liver abscesses, was admitted Dec. 29, 1937, and discharged Feb. 25, 1938. Three days prior to admission he began to experience generalized abdominal pain of increasing severity. The next day two shaking chills occurred. The following day generalized pain and pain in the right lower quadrant became more severe. On admission the temperature was 101.2 F. and the pulse rate 120. Tenderness and rigidity were present in the right lower quadrant of the abdomen. The diagnosis was acute appendicitis with diffusing peritonitis. Appendectomy and drainage were performed for acute gangrenous ruptured appendicitis with diffusing purulent peritonitis. (Culture of peritoneal pus yielded *Bacillus coli*.) For the first week the temperature ranged from 101 to 102 F. On the ninth day there were a sudden rise of temperature to 103 F., jaundice and chilly feelings. On the tenth day there was a definite shaking chill. From the tenth to fifteenth day there was definite jaundice. The icteric index was 22 (acetone method). The white blood cells numbered 23,600 with polymorphonuclear leukocytes 88 per cent. For three weeks the patient experienced a septic type of fever, the temperature rising to 104 F. almost daily, frequent chills and progressive tender enlargement of the liver. During this period, blood cholesterol was very low (from 80 to 95 mg. per hundred cubic centimeters), with only traces of cholesterol ester. Sulfanilamide therapy was started twenty-four days after the onset of the septic symptoms. Two days after the beginning of this therapy exploratory laparotomy was done because of progressive tenderness in the right upper quadrant, which seemed to point to liver abscess. Microscopic section of the liver taken at biopsy is shown here.

At operation the liver was found to be grossly and uniformly enlarged by approximately 30 per cent of its normal size. The surface was smooth and the color mottled and a dark purplish red. Palpation revealed the subphrenic space entirely clear. The organ was extremely soft. There were innumerable nodular masses, approximately 2 cm. in diameter, scattered throughout the substance of the liver, presumably multiple small liver abscesses. The substance of the liver was extremely friable, as was evidenced when passage of the palpating hand was made over the left lobe of the liver and traction on the ligamentum teres caused an inadvertent rent in the anterior margin of the liver.

No therapeutic procedure being possible, a biopsy specimen approximately 1.5 cm. in diameter was taken from the margin of the traumatic rent in the liver, as already noted. Bleeding was controlled by the passage of a widely placed plain catgut suture passed with the blunt "liver" needle. Aspiration of the gallbladder for chemical analysis for the content of sulfanilamide was then done by passing the aspirating needle through the right lobe of the liver to enter the gallbladder on its superior nonperitonealized aspect. Here there was no possibility that bile would leak into the peritoneal cavity through the site of puncture of the gallbladder. Ten cubic centimeters of dark bile was withdrawn to be analyzed for its content of sulfanilamide. (This was later reported as 2.5 mg. per hundred cubic centi-

mers.) Aspiration of the liver substance was then done for bacteriologic culture. (This culture showed no growth.) Closure of the laparotomy wound was then done in the usual manner.

Sulfanilamide therapy was continued (6 Gm. the first day, 5 Gm. the second day, and 4 Gm. a day thereafter until the patient had been afebrile for two weeks; then 2 Gm. a day for one week further). Three days after the biopsy (five days after the beginning of the sulfanilamide therapy) the temperature had declined by lysis, and it remained at the level of from 99 to 100 F. for several weeks. It remained normal for ten days after the cessation of sulfanilamide therapy. The patient was then discharged. The hemoglobin content, white blood cell count and granulocyte count were closely watched throughout the course and at no time showed a noticeable depression.



Microscopic section of biopsy specimen taken from the liver in case 2, demonstrating endophlebitis with beginning thrombosis of intrahepatic portal radicles and perivenous abscess formation. (Dr. Paul Klemperer.)

During the course of sulfanilamide therapy chemical analysis of the blood revealed a sulfanilamide concentration of 6 mg. per hundred cubic centimeters.

SUMMARY AND CONCLUSIONS

Two patients with suppurative pylephlebitis and liver abscesses recovered under sulfanilamide therapy. In the first case, the diagnosis was purely clinical, since exploratory laparotomy was not done. In the second case, the diagnosis was proved by biopsy of the liver at an exploratory operation. Examination of the biopsy revealed endophlebitis of the intrahepatic portal radicles and perivenous liver abscesses, shown in the microscopic section. The infection in this case was due to the colon bacillus, an organism known to be susceptible to sulfanilamide therapy.¹³

From this experience we believe that a further trial of this form of therapy in these otherwise almost hopeless cases is warranted.

1112 Park Avenue—23 East Seventy-Fourth Street.

13. Helmholz, H. F.: Bactericidal Power of Urine After Administration of Sulfanilamide by Mouth, *Proc. Staff Meet., Mayo Clin.* 12:244 (April 21) 1937. Buttle, Parrish, McLeod and Stephenson.¹³

Special Article

THE PATHOLOGY OF VITAMIN C DEFICIENCY

GILBERT DALLDORF, M.D.

VALHALLA, N. Y.

This article and others recently published or to be published comprise a new series on the present status of our knowledge of the vitamins. They have been prepared under the general auspices of the Council on Pharmacy and Chemistry and the Council on Foods. The opinions expressed are those of the authors and not necessarily the opinions of either council. Reprints are not available but the articles will be published later in book form.—Ed.

The primary morphologic effects of vitamin C deficiency occur in the intercellular substances of certain mesenchymal derivatives. These can best be described in terms of the prototype of these structures, loose connective tissue. Under normal conditions the type cell, the fibroblast, lies in an amorphous ground substance within which fibrils (reticulum) are formed which may in turn become gathered into wavy bands of collagen. In this transformation the fibrils seem to become cemented together by a translucent matrix, the formation suggesting a colloid phenomenon, the setting of a gel. It is precisely this phase of the formation of intercellular materials which may be completely controlled by vitamin C. Thus in guinea pigs which have been depleted of vitamin C the ground substance and fibroblasts are present as in health but fibrils or collagen are not formed. When the deficiency is satisfied, translucent bundles and masses of collagenous materials reappear within eighteen hours. The formation of intercellular material of bone (osteoid tissue) and of teeth (dentin) may be similarly controlled by withholding or supplying vitamin C.

These changes have been accurately studied¹ and observed by various pathologists. The observations on experimental animals are in perfect harmony with the observations of spontaneous scurvy in man.² A point that is still disputed is whether the vitamin directly affects the intercellular colloids or the cells. Collagen may form in the absence of fibroblasts,³ but in the primary response to treatment in scurvy the newly formed material is seen in proximity to the fibroblasts or their processes.⁴ While the cells are not significantly altered in appearance when the phenomena just described are taking place, they are altered during the late stages of chronic scurvy. Decision must be reserved on this point. Because the vitamin is assumed to have a pronounced effect on oxidation-reduction phenomena in the tissues and because hydrogen ion concentration is of critical importance to colloidal systems, it is tempting to accept the simpler explanation that the vitamin directly alters the physical character of the intercellular fluids.

Defective intercellular substances are seen in connective tissue, bones and teeth and are believed to

occur in the blood vessels. An interesting modification of the process is apparent in partial deficiency, wherein a substitute material forms in the teeth in place of dentin. This has been spoken of as "osteodentin," since it resembles both materials. Similarly, in the bones, collagenous material appears in partial deficiency in place of osteoid. The tendency is for defective materials to form in connective tissue in partial depletion, and for nothing of a substantial nature to form in complete depletion. Further involution of the tissues in complete deficiency does not occur because the animals die.

Morphologic changes have not been detected in the capillaries and it is doubtful whether they occur. Capillaries originate from embryonic connective tissue and it is not surprising that they are affected. But where the weakness occurs is unknown. The endothelium of capillaries is believed to be fused together by a cement substance, but the capillary is also accompanied and surrounded by connective tissues and thin collagenous fibers ensheath the endothelium. Whether the effect of the deficiency is on the sheath or on the endothelial cement substance has never been decided. As in the case of the connective tissues the parenchymal cells appear to be normal and may multiply. Thus in young granulation tissue during depletion capillary budding has been seen; but this attempt at regeneration is soon aborted, presumably by lack of intercellular materials.⁵

The anatomic manifestations of scurvy are greatly modified by two factors, growth and stress. These are of such importance to the pathology of vitamin C deficiency that they must be discussed in some detail.

Growth so modifies the anatomic picture in scurvy that for 200 years the disease in children and infants was considered a variety of rickets, a condition which it superficially resembles more closely than it does adult scurvy. Hematomas become less and less frequent as the age of the patients increases. It is in the young, growing animal that bone pains occur; in the adult they are rare. Osteoporosis is greatly intensified in the young animal, just as it is always most pronounced at the particular part of the bone where growth is most active. Moreover, the most rapidly growing bones at the particular age at which scurvy occurs are most affected. This distribution and exaggeration of the lesions are similar to what occurs in rickets.

Stress modifies the site of the lesions and determines the extent and involvement of the various structures. Individual lesions can best be understood if the lines of force are borne in mind. Stress plays a major part in determining the site of the hemorrhages; the pressure of boots or a diaper, the location of a vessel near a bony prominence—these are the factors which determine whether or not hemorrhages will occur. The hemorrhages and other changes in muscles depend on stress.⁶ In olden days it was noticed that blacksmiths and wool carders developed lesions in the shoulders and arms, soldiers in the calf and lumbosacral muscles.⁶

Lesions are indirectly modified by other factors, for example the presence or absence of a variety of other diseases (the list is long and rapidly growing and includes many infectious diseases, lobar pneumonia, typhoid and tuberculosis among others) and disturbances associated with an increased metabolic rate. These may operate similarly to growth and physical

From the Laboratories of Grasslands Hospital.

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stress (activity) in determining the requirements of vitamin C and therefore, indirectly, the extent and degree of the scorbutic lesions. It would be instructive to determine whether the vitamin enters directly into inflammatory phenomena. There is substantial evidence to support the view that it is essential to the formation of blood cells,⁷ including the granular leukocytes, and in this manner at least may be consumed at a higher than normal rate during infectious disease. Review of the larger series of cases of scurvy strongly encourages the belief that severe infectious diseases and scurvy go hand in hand and that each influences the severity and duration of the other.⁸

If the influence of growth and stress is borne in mind, the individual lesions of scurvy may be described without note being taken of modifications and exceptions that may or may not occur because of these influences.

BONES

Skeletal lesions are commonest in the costochondral junctions, the distal end of the femur, the proximal end of the tibia, femur and wrist. The distal humerus and proximal ulna are usually spared. In the affected regions bone formation (enchondral bone growth) ceases and the existing osseous shell becomes rarefied, widened and conical. The epiphysis is not affected, at least in early stages, but may become displaced. False motion occurs in advanced cases and probably in even moderately severe cases in the costochondral junctions of the ribs. Microscopic examination reveals a rarefaction of the existing cortex, cessation of bone growth and replacement of the normal junction by a zone of collagen-poor connective tissue in which are embedded fragments of densely calcified cartilage matrix, bare of osteoid tissue. In controlled material it has been shown that the connective tissue cells of the marrow are migrated osteoblasts which have reverted to fibroblasts. The process suggests that in the absence of vitamin C the osteoblasts, unable to form osteoid tissue, revert to their prototype and attempt to form a fibrous union between diaphysis and epiphysis. This zone is generally spoken of as the "gerüstmark," or framework marrow, and in it lie the densely calcified fragments of cartilage matrix and bony trabeculae which are so conspicuous in roentgenograms. This is also the classic anatomic lesion of scurvy and may be found, in infants and children, in early or moderately advanced cases of the disease although frequently several bones must be searched. Frequently this kind of lesion is complicated by hemorrhages, either large subperiosteal ones or small ecchymoses within or along the bone. In incompletely developed lesions, hemorrhages may be the deciding factor in an anatomic diagnosis.

If suspiciously enlarged costochondral junctions are submitted to microscopic examination, various stages of the typical scorbutic lesion will frequently be found. It is not necessary that it be fully developed. Experience rapidly recognizes a general fragility of the connective tissue fibers, a suggestive watery zone about the older osteoblasts and a defective osteoid tissue formation which plainly indicate the presence of scurvy. The greatest difficulties occur when scurvy is complicated by other diseases, for example rickets. It is at times difficult to distinguish scurvy from other dystrophies of bone such as osteogenesis imperfecta. Some of the latter conditions may indeed be related to the supply of vitamin C.

The periosteum shows a weakening of its attachment and a furious effort of connective tissue cells to reinforce it. This is most apparent at muscular attachments. Periosteal lesions of all degrees are prone to be complicated by hemorrhages due to the unyielding nature of the bone.

TEETH

In the teeth of adults with scurvy the dentin is seen to be resorbed and porotic. This process commences about Tomes's canals. The little replacement dentin that may be formed is inferior in appearance (osteodentin). In the pulp, chiefly about the vessels, atrophy, hyperemia, degeneration of the odontoblasts, the formation of small cysts and foci of calcification occur. The lesions develop first in the apex of the tooth and the bifurcation of the root canal. The fluid ground substance noted in experimental scurvy has also been observed in human material. The cementum is similarly affected.⁹

In the incisor teeth of the guinea pig early and extensive changes occur, because of the continuous rapid growth of these structures. In the guinea pig partial deficiency results in the formation of "osteodentin" and complete deficiency in undifferentiated matrix. In both cases the odontoblasts migrate from the predentin and revert to simpler types. Fish and Harris¹⁰ demonstrated defects in enamel and cementum as well as in dentin.¹¹

GINGIVA

Lesions of the gingiva occur only when teeth are present and are most severe about deformed or broken teeth. The gums become swollen and boggy and bleed easily. In severe cases of scurvy they have become so large as to hide the teeth and make mastication painful and difficult. Rarefaction of the alveolar bones results in loosening of the teeth. The gingival lesions commence on the papillae, first as a hyperemia with dilated, thin walled vessels with a tendency to intractable hemorrhage. Disintegration of the epithelium follows and infection with ulceration, granulations and even gangrene. Lesions in the mouth are remarkably constant. Indeed, fifty years ago scurvy was defined as a generalized, afebrile disease accompanied by symptoms of fatigue, hemorrhages, usually starting on the legs, and changes in the gums.

MUSCLES

In severe scurvy, now rarely seen except in experimental animals, severe changes occur in the muscles. Fragmentation of the striated fibers and intense reparative efforts marked by multiplication of the sarcolemma occur. If the scurvy is prolonged, replacement by connective tissue poor in collagen may be seen. Höjer considered these lesions plus metastatic calcification characteristic of scurvy but they have since been reported¹² in various other experimental deficiencies (although without the calcification which is by no means constant in scurvy). If such muscle changes are accompanied by spontaneous hemorrhages they would seem to constitute strong evidence of the pres-

9 Westin, G.: Ueber Zahnveränderungen in Fällen von Skorbut bei Homo. Stockholm, Fahlcrantz, 1931.

10 Fish, E. W., and Harris, L. J.: The Effects of Vitamin C Deficiency on Tooth Structure in Guinea Pigs, Brit. Dent. J. 58: 3 (Jan. 1) 1935.

11 The reader is referred to the report by Fish and Harris¹⁰ for a divergent interpretation of the pathogenesis of scurvy as well as for an excellent description of the lesions in the teeth of guinea pigs. The view of Fish and Harris, similar to that advocated by Höjer, is that the primary effect of deficiency is an atrophy of the parenchymal cells. In my opinion this theory fails to explain the phenomena or complete deprivation already referred to and applies only to the late, nonspecific effects.

12 Goetsch, M., and Pappenheimer, A. M.: Nutritional Muscular Dystrophy in the Guinea Pig and Rabbit. J. Exper. Med. 54: 145 (Aug.) 1931. Wollach, S. B.: The Pathologic Changes Resulting from Vitamin Deficiency, J. A. M. A. 108: 7 (Jan. 2) 1937.

7 Parsons, L. G., and Hawksley, J. C.: The Anhaematopoietic Anaemias, Arch. Dis. Childhood 8: 117 (April) 1933.

8 Nassau, E., and Singer, M. J.: Zur Kenntnis des Vorstadiums der Barlow'schen Krankheit, Jahrb. f. Kinderh. 98: 44, 1922.

ence of scurvy, especially in man, since typical lesions of the kind have been reported in human cases of scurvy but not, to our knowledge, in other instances of human avitaminoses.

EYES

In severe scurvy, bloody tumors of the conjunctiva and ecchymoses of the eyelids and elsewhere about the eyes may appear. The other eye lesions that have been reported in the past are now known to be the results of simultaneous vitamin A deficiency (degeneration of the cornea, pigmentation and night blindness).

SKIN

The skin is of particular interest because of the frequency of signs of the disease there and the clue such easily observable lesions give to the general status of the patient's vitamin C supply. The lesion of the skin that is characteristic of scurvy is the perifollicular or petechial hemorrhage. This is commonest on the lower extremities or wherever pressure exposes the weakness of the capillaries. In the epidemics of a hundred years ago much was made not only of the presence of the perifollicular hemorrhage but also of changes in the follicle itself,¹³ keratosis, dilated follicle mouth and fragmentation or loss of hair. Frequently dark, grayish pigmentation also was described. Identical observations were made during the World War.² As we now know, these were cases of combined deficiency of vitamins A and C. However, these observations raise the point whether similar perifollicular effects occur in uncomplicated scurvy, since it might otherwise seem that the presence of a diseased follicle, especially a thickened, hard one, would of itself predispose to hemorrhage. Undoubtedly similar lesions occur about normal hair follicles, as we have ourselves observed and other reports suggest, and have been absent in outspoken cases of vitamin A deficiency.¹³

OTHER LESIONS

Effusions, often blood stained, are common in the serous cavities. There may be slight edema about the ankles. Enlargement of the heart may occur. Circulatory collapse seems to have been a feature of the scurvy seen a hundred years ago and has been noted occasionally since. Whether there is a counterpart of the skeletal muscles lesions in the cardiac musculature, as Höjer believed, is doubtful. I have seen no such lesions, although fatty degeneration is common. Dilatation of the heart occurs. Atrophy of the bone marrow occurs in scurvy, and Wolbach¹² reports in experimental cases large areas of an amorphous material resembling amyloid. Except for this nothing characteristic has been reported, although the anemia of scurvy responds specifically to vitamin C.¹⁴ The gastrointestinal tract is largely spared. Minute hemorrhages may be found and even larger ones with secondary necrosis or ulceration (in experimental scurvy),¹⁵ but the study of human material does not support the view that the gastrointestinal tract suffers in a conspicuous fashion from vitamin C deficiency.

The adrenals atrophy in chronic scurvy as the absorption of cortical fat and vitamin C progresses.¹⁶ In

the early stages they are swollen and hyperemic. The presence of vitamin C in the adrenal cortex may be easily demonstrated by soaking the split organ in silver nitrate, a procedure which is useful in the autopsy room.

Atrophy of the lymphatic tissue and to a lesser extent of other organs, especially glands of internal secretion, occurs but seems due to the general effects of debility.

CORRELATION OF LESIONS AND VITAMIN SUPPLY

It would be of considerable value to determine the various levels of vitamin C deficiency associated with these morbid manifestations, and to a certain extent this may be done. It is known, for example, that the first morbid effect of a severe depletion is capillary fragility¹⁷ and probably also that the only morbid effect of a very slight negative vitamin C balance is capillary fragility or the presence of petechiae. Lind¹⁸ himself said of the petechiae that they are the most constant symptom of all and occur even in the mildest cases, that they may indeed be the sole symptom and that in such cases their presence is sufficient for the diagnosis of scurvy. All recent work has served but to confirm this view. In human scurvy these changes are preceded only by a short prodrome of from five to eight days of weakness and lassitude. Petechiae then, of skin or nose or other cavities, are the first morbid expression of vitamin C deficiency and are related to what has recently been spoken of as subclinical scurvy. In this condition capillary fragility is present. Chemical tests reveal a subnormal vitamin C concentration in fasting blood samples. A state of unsaturation is evinced by measurements of the blood concentration and urinary excretion after a test dose of ascorbic acid.¹⁹ The earliest stages of unsaturation are as a rule associated with morbid capillary resistance. Subclinical scurvy therefore appears to be definitely a pathologic state, albeit the deviation from health is slight. This degree of vitamin C deficiency is seldom recognized radiographically and with difficulty, if at all, by anatomic study. A comparable degree of deficiency in the guinea pig is uniformly associated with definite lesions in the incisors.

In moderately advanced scurvy the chemical tests reveal distinctly abnormal values and considerable vitamin C is required to saturate the patient. In such cases the hemorrhages may be large, commonly subcutaneous ecchymoses or hematomas. It is a general rule in scurvy that the more severe the disease the more extensive the hemorrhages and the more likely is hemorrhage from larger vessels. In this degree of deficiency skeletal lesions are present and will be found if the search is thorough. The study of Park and his colleagues gives us a clue to the relative efficiency of methods of diagnosis. Of eighteen cases of scurvy in young children only two were diagnosed clinically and only six at routine postmortem examination, yet all had distinct lesions.²⁰

In severe scurvy nearly complete unsaturation may be demonstrated by chemical tests. The initial doses

13. Frazier, C. N., and Hu, C. K.: Nature and Distribution According to Age of Cutaneous Manifestations of Vitamin A Deficiency, *Arch. Dermat. & Syph.* 33: 825 (May) 1936.

14. Mettler, S. R., and Chew, W. B.: The Anemia of Scurvy: Effect of Vitamin C Diet on Blood Formation in Experimental Scurvy of Guinea Pigs, *J. Exper. Med.* 55: 971 (June) 1932. Höjer, J. A.: Studies in Scurvy, *Acta paediat. (supp.)* 2: 8, 1924.

15. Smith, D. T., and McConkey, Mack: Peptic Ulcers (Gastric, Pyloric and Duodenal): Occurrence in Guinea Pigs Fed on a Diet Deficient in Vitamin C, *Arch. Int. Med.* 51: 413 (March) 1933.

16. Bessey, O. A.; Menten, M. L., and King, C. G.: Pathologic Changes in the Organs of Scurbic Guinea Pigs, *Proc. Soc. Exper. Biol. & Med.* 31: 455 (Jan.) 1934.

17. Dalldorf, Gilbert: Criterion of Hemorrhagic Diathesis in Experimental Scurvy, *J. Exper. Med.* 53: 289 (Feb.) 1931.

18. Lind, J.: A Treatise of the Scurvy, ed. 3, London, S. Crowder, 1772.

19. Sloan, R.: A Comparison of Methods for Detecting and Grading Subclinical Scurvy, *J. Lab. & Clin. Med.*, to be published. Harris, L. J., and Ray, S. N.: Diagnosis of Vitamin C Subnutrition by Urinalysis, *Lancet* 1: 71 (Jan. 12) 1935. Archer, H. E., and Graham, George: Some Observations on the Excretion of Ascorbic Acid, *Lancet* 1: 710 (March 28) 1936. Abt, A. F.; Farmer, C. J., and Epstein, I. M.: Normal Cavitic (Ascorbic) Acid Determinations in Blood Plasma and Their Relationship to Capillary Resistance, *J. Ped.* 8: 1 (Jan.) 1936.

20. Park, E. A.; Guild, H. G.; Jackson, D., and Bond, M.: The Recognition of Scurvy with Especial Reference to the Early X-Ray Changes, *Arch. Dis. Childhood* 10: 265 (Aug.) 1935.

of vitamin, even when large, promptly are absorbed from the blood stream and little is lost in the urine. Hemorrhages are extensive and skeletal and gingival lesions outspoken.

CONCLUSIONS

It may safely be concluded therefore that the anatomic effects of vitamin C deficiency are very prompt to appear, certainly in the young, and that they occur, if the vascular changes are included, even in the mildest degrees of deficiency. Since clinical reports agree that subclinical scurvy, whether on the basis of chemical tests or measurements of capillary strength, is common, it may be assumed that morphologic stigmas due to the same deficiency are likewise common. However, both clinical and anatomic identification of scurvy remains, as it always has been, a matter of alertness on the part of the physician.

Finally, it may be pointed out that the recently acquired understanding of the scorbutic process affords pathologists and biologists a useful tool in the study of disturbances of intercellular materials. It should be of value also in the study of similar changes in senility.

Council on Physical Therapy

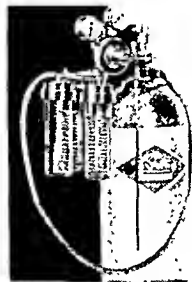
THE COUNCIL ON PHYSICAL THERAPY HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORT.

HOWARD A. CARTER, Secretary.

OHIO OROPHARYNGEAL CATHETER OUTFIT ACCEPTABLE

Manufacturer: Ohio Chemical and Manufacturing Company, Cleveland.

The Ohio Oropharyngeal Catheter is designed for the therapeutic administration of oxygen. It is a portable unit consisting of a multistage regulator with a gage of maximum pressure reading 3,000 pounds per square inch, a liter gage, a humidifier, one length of rubber tubing, a tapered nipple, one rubber nasal catheter, an adjustable wrench, a syringe for filling water jars, a tube of lubricating jelly and an adapter. The three wheel cylinder truck is optional. The multistage regulator has been approved by the Underwriters' Laboratories. It is supplied with screw connection fitting cylinders used for industrial purposes but may be adapted to tanks used for medical purposes. The humidifier consists of two water jars and a trap jar, so constructed that the oxygen passes through each in succession. A water level is indicated on the jars. The size of the water jars obviates frequent fillings. When higher rates of flow are used, the trap prevents water



Ohio Oropharyngeal Catheter.

from passing into the tubing and hence into the patient's throat. The firm claims that the humidifier delivers a high concentration of oxygen, properly humidified, continuously over long periods of time.

The unit was investigated in a clinic acceptable to the Council and appeared to be satisfactory on the whole. However, the flow meter was not accurate for a small flow of 2 liters per minute. Of course, proper clinical use is guided by the patient's needs more than by the meter when flows under 6 liters per minute are used. For flows of 4 and 6 liters it was accurate.

Since the reducing valve and humidifier are satisfactory, the flow meter gage effective for most clinical purposes, and the rubber tubing of good nonkinking variety, the unit is considered satisfactory for clinical use.

In view of the foregoing report, the Council on Physical Therapy voted to include the Ohio Oropharyngeal Catheter Outfit for oxygen therapy in its list of accepted devices.

Council on Foods

ACCEPTED FOODS

THE FOLLOWING PRODUCTS HAVE BEEN ACCEPTED BY THE COUNCIL ON FOODS OF THE AMERICAN MEDICAL ASSOCIATION AND WILL BE LISTED IN THE BOOK OF ACCEPTED FOODS TO BE PUBLISHED.

FRANKLIN C. BING, Secretary.

(1) NUTRADIET BARTLETT PEARS PACKED IN WATER

(2) NUTRADIET QUARTERED BARTLETT PEARS PACKED IN WATER

Distributor.—The Nutradiet Company, a subsidiary of S & W Fine Foods, Inc., San Francisco.

Description.—Canned, peeled, halved and quartered Bartlett pears packed in water without added sugar.

Manufacture.—Bartlett pears are washed in hydrochloric acid to remove the residue of lead arsenate, which is used as a spray, are peeled by machinery and by hand, cut in halves or quarters, and the cores and stems are removed. The fruit is soaked in a 3 per cent salt solution, rinsed in running water and packed in cans. Water is added and the cans are heated to 71 C. for six minutes in the presence of steam, sealed and processed for twelve minutes in boiling water.

Analysis (submitted by manufacturer).—Moisture 90.3%, total solids 9.7%, ash 0.16%, fat (ether extract) 0.07%, protein (N \times 6.25) 0.2%, crude fiber 0.6%, carbohydrates other than crude fiber (by difference) 8.5%, titratable acidity as citric malic acid 0.2%.

Calories.—0.35 per gram; 10 per ounce.

Claims of Manufacturer.—For diets in which sweetened fruit is proscribed.

MRS. PALEY'S BABY FOOD—STRAINED MIXED VEGETABLES WITH SOYA BEAN, DICAL- CIUM PHOSPHATE AND WHEAT GERM

Manufacturer.—Paley-Sachs Food Company, Houston, Texas.

Description.—A combination of cooked vegetables including carrots, potatoes, celery, tomato purée, cabbage, soya beans, wheat germ, onions and added dicalcium phosphate.

Manufacture.—The vegetables are prepared as for Mrs. Paley's Baby Food—Strained Vegetable Soup with Beef Broth and Cereal (THE JOURNAL, Sept. 17, 1938, p. 1101). Wheat germ is pressure cooked with the prepared vegetables in formula proportions, and definite amounts of dicalcium phosphate are added. The mixture is sieved, filled into jars, vacuum sealed and heat processed.

Analysis (submitted by manufacturer).—Moisture 81.5%, total solids 18.5%, ash 1.5%, fat (ether extract) 0.8%, protein (N \times 6.25) 4.4%, reducing sugars as dextrose 0.5%, sucrose 1.1%, crude fiber 1.1%, total carbohydrates other than crude fiber (by difference) 10.7%, calcium (Ca) 0.246%, phosphorus (P) 0.137%, iron (Fe) 0.003%.

Calories.—0.7 per gram; 20 per ounce.

DEXTROSE, KARO BRAND

Manufacturer.—Corn Products Refining Company, New York.

Description.—U. S. P. dextrose.

Manufacture.—Raw kernels of corn are softened by steeping in a warm bath containing a small amount of sulfur dioxide. The starch, separated from the other constituents, is hydrolyzed with hydrochloric acid and the resulting liquor is filtered, clarified, concentrated and crystallized. The first yield is recrystallized from water. The method of manufacture is covered by patents numbered 1508569 and 1559176.

Analysis.—Ash 0.096%; moisture 7.87%; optical activity + 52.63°; chlorides, trace; starch, absent; erythrodextrin, trace.

Calories.—3.7 per gram; 104 per ounce.

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SATURDAY, OCTOBER 8, 1938

THE EXPERIMENTAL PRODUCTION OF OVULATION

Periodically a graafian follicle ripens and ruptures, and the ovum escapes. The ruptured follicle then develops into a corpus luteum, a gland of internal secretion which is necessary for the implantation of the fertilized ovum. These brief facts barely outline the immensely complicated story of ovulation. No one has actually seen a graafian follicle rupture nor has any one heretofore succeeded in producing ovulation in women. Theoretically, the ideal substances for this purpose would be certain extracts of the anterior lobe of the pituitary gland, but these have not been available in a sufficient state of purity. Gonadotropic substances derived from the urine and blood of pregnancy have failed to produce any consistent changes in ovarian activity when given parenterally.

Recently a gonadotropic substance has been found in the serum of pregnant mares and sufficiently purified, it is thought, to bring about ovulation in women. This substance was first observed by Cole and Hart¹ in 1930 in high concentration in the serum of pregnant mares. Experiments have shown that its action closely resembles that of pituitary extracts. It produces ovulation, luteinization and follicle stimulation. It is not soluble in the usual fat solvents used for the isolation of estrogenic substance. A highly purified preparation of this gonad-stimulating principle was prepared by Cartland and Nelson,² and biologically assayed.

Some unusual observations of the effects of this substance have been made by Davis and Koff³ at the University of Chicago and the Chicago Lying-In Hospital. After preliminary experimental work with this

gonadotropic fraction obtained from the serum of pregnant mares, they administered it intravenously to thirty-six women who were awaiting abdominal operations for a variety of pathologic conditions. These women were first carefully tested for protein sensitization. They were mostly at the period of life when there is a rapid decrease of activity of the ovaries; others in the group were suffering from pathologic conditions which would mask any results that might be obtained. The gonadotropic substance was given intravenously on varying days of the menstrual cycle; then the ovaries of these women were observed later when they came to undergo laparotomies.

It was observed that ovulation had occurred recently in about half of the women to whom this substance had been given. The evidence was obtained not merely by gross inspection of the ruptured follicles but also by microscopic examination. The studies made of these ovaries revealed corpora lutea present in earlier stages than had ever before been described. Careful comparison indicated that most of these corpora lutea were less than eighteen hours old and well within the time that elapsed between the administration of the gonadotropic substance and the time the ovary was removed. It has been considered heretofore that the process of ovulation in the human being extended over a period of several days or longer. The time that elapsed from the administration of the gonadotropic substance until ovulation in these patients was unusually short. The authors² believe that this substance is capable of causing rapid follicle growth; apparently, under this influence, the follicles ripen, rupture, release their ova and are converted into corpora lutea all within twenty-four to thirty-six hours.

The clinical application of this experimental work presents problems. The significance of some of the observations is not well understood. Heretofore the clinical administration of gonadotropic substances has met with little success. Now, however, an abundant source of supply and a highly purified product are available. Biologically this gonadotropic substance resembles extracts and implants of the anterior lobe of the pituitary. It differs biologically and chemically from all other gonadotropic substances studied. Unlike the gonadotropic substance in the blood and urine of pregnant women, the fraction from mare serum is not excreted in the urine at any time during gestation; unlike substances derived from the urine of pregnancy, it is not filtrable through collodion membranes. Mare serum hormone apparently is a peptide.

Much more experimental work is necessary before the clinical application of this product can be adequately defined. Its use under very carefully supervised conditions may prove to be efficacious, however, in the treatment of patients in whom ovulation and follicle growth are at fault.

1. Cole, H. H., and Hart, G. H.: *Am. J. Physiol.* 93:57 (May) 1930.

2. Cartland, G. F., and Nelson, J. W.: *J. Biol. Chem.* 119:59 (June) 1937.

3. Davis, M. E., and Koff, A. K.: *The Experimental Production of Ovulation in the Human Subject*, *Am. J. Obst. & Gynec.* 36:183 (Aug.) 1938.

ARTHRANOL—ANOTHER "CURE" FOR ARTHRITIS

The greater the number of persons with a certain disease, the greater the number of remedies offered for treatment. One of the most lucrative of all fields is arthritis. The results of treatment of arthritis and rheumatism are easily susceptible to misinterpretation; the condition is subject to numerous remissions and relapses. Small wonder, then, that as many products are offered for sale with little or no evidence of their usefulness. Frequently products for the treatment of arthritis are exploited indirectly to the public by newspaper and periodical publicity planned to follow the presentation of a paper at some scientific gathering. The ridiculously optimistic claims advanced by Seydel for a benzoate type of product called Subenon were widely publicized after the meeting of the American Chemical Society two years ago. To the credit of the American Chemical Society, it promptly took effective action to prevent repetition of such impositions in the future. More recently other manufacturers have attempted to exploit the profession and the public with promotion of high potency vitamin preparations and various colloidal preparations for use in "rheumatism." The patient with arthritis grasps at every straw in the hope that long treatment may be avoided—that at last some specific method has been discovered whereby he may recover full health and vigor. Naturally any announcement that such a startling discovery has been made appeals to a large proportion of the public. The premature release of misinformation does harm.

The current example of such unwarranted exploitation in the field of medicine is "Arthranol." The product has been available for about three years. In *Time*, September 26, appeared the statement:

Last week at a meeting of the Atlantic County Medical Society, 60 year old Dr. Samuel Stern of Atlantic City announced that he had successfully used a new drug, Arthranol, for the treatment of arthritis. Arthranol is a highly complex salt made from a nitrogen compound, phosphorus and iodine.

When such announcements are published, the effects are promptly felt in the offices of the American Medical Association. Physicians and laymen alike inquire concerning the composition of Arthranol and seek opinion of its value. This product is marketed by the Atlantic Research Foundation, whose president and director is Dr. Stern. In 1936 the Council on Pharmacy and Chemistry was informed that the foundation was established as a nonprofit organization to provide the proper handling of products, all income to be devoted to further medical research. It was also stated that the foundation has charged a fee of \$3 for each box of Arthranol. An announcement appeared in 1936 in the lay publication *Modern Mechanics & Inventions Magazine* that "arthritis and rheumatism, two of humanity's most common afflictions, are now believed to be under control as the result of a new serum developed by

Dr. Samuel Stern of Atlantic City, N. J., and William Kurland, chemist." There was also a picture of Dr. Stern and William Kurland standing in front of a laboratory desk overcrowded with microscopes and other chemical apparatus. It was stated that the serum has proved successful in 97 per cent of 125 cases. Now, two and one-half years later, Dr. Stern states, according to *Time*, that Arthranol¹ has been given to practically twice the number of patients (250) and that 90 per cent of these patients were relieved. Maybe if one were to extrapolate a curve for 1,000 patients, the number of "relieved" would be less than 48 per cent, as the later report indicates the product was less effective in the next 125 patients!—all of which goes to show that the figures may mean little. In reply to a request for information in 1936, Dr. Stern stated: "The new chemical compound consists of ammonia, 26.1 per cent, phosphorous 4.7 per cent, and iodine 69.2 per cent." This statement, of course, was entirely inadequate. He also wrote: "It is administered hypodermically 1 cc. to a dose in buffered isotonic solution. We have tried Locke, Ringèr and other menstra, and at present we are using a 5 per cent dextrose with $\frac{1}{4}$ per cent chloretone as a menstra, having found it is less painful and probably more efficient than the other menstra we have previously used. As to literature, reports etc., no reports have been made to date as we are still collecting data and pursuing our researches." Last week an inquiry was telegraphed to Dr. Stern asking again about the composition of the product and about the literature. In the circular that accompanied Dr. Stern's reply the product was described as "amino-phospho salicyl, Benzoyl, iodide." Dr. Stern gave the following composition for the product:

Average Analysis of Arthranol Per Cent		
Total ammonia.....	(NH ₃)	15.02071
Ammonium phosphate di-basic.....	(NH ₄) ₂ HPO ₄	24.9165
Ammonium iodide.....	(NH ₄)I	3.1887
Ammonium chloride.....	(NH ₄)Cl	9.7030
Ammonium benzoate.....	(C ₆ H ₅) ₂ CO.O.NH ₄	32.5290
Ammonium salicylate.....	(C ₆ H ₄) ₂ (OH).CO.O.NH ₄	20.0390
Water		9.0000

The fourth decimal point for such "average" figures is not significant.

The statement of composition indicates that there is nothing wonderful in the preparation; the product apparently is not of the same composition as that stated in 1936. The largest component seems to be ammonium benzoate, which years ago was generally discarded in the treatment of "rheumatism" in favor of the more valuable salicylates. Over half the mixture, according to the information given, consists of ammonium benzoate and ammonium salicylate. Alkali iodide, another ingredient, has been used for years in certain forms of arthritis. The composition of Arthranol does not warrant the optimistic claims made for it. All the active ingredients have, in fact, been employed many times before.

1. Also spelled Arthronol.

Rather naively Dr. Stern further states:

Now, as to literature at this writing I have none except a mimeograph sheet of instructions for the use of our remedy which I am enclosing. I am in hopes to receive from the printer shortly reprints of the paper I presented before the Atlantic County Medical Society. I am taking this step in having reprints made in advance of the publication of this article in order to supply the immediate demands for an accurate knowledge of the claims I am making.

Please understand that we are most willing and anxious to give any information whatsoever that you or the profession may desire.

Our research laboratories are straining every effort to supply the demand of this article but I fear it will be impossible. I am endeavoring to license a responsible manufacturer to produce this product, of course, it shall be upon strictly proper and ethical lines. I am in hopes to be able to complete this very shortly, in the mean time, I will strain every point to meet the demands that are being made upon me.

This is not the first time such publicity has been attached to Dr. Stern. A clipping from the *New York City Telegram*, Nov. 10, 1923, states:

New Diabetes Treatment

Atlantic City, Saturday.—A new treatment for diabetes and acidosis, in the form of a cream, which it is claimed can be applied externally and absorbed to neutralize poisonous acids was announced by Dr. Samuel Stern of this city, speaking before the Atlantic County Medical Society.

Today no one hears of his treatment for diabetes; fifteen years hence will any one hear of Arthranol?

Current Comment

YELLOW FEVER VIRUS IN JUNGLE MOSQUITOES

In 1935 THE JOURNAL called attention¹ to the important implications resulting from the investigation of yellow fever in the Valle do Chanaau, Esperito Santo, Brazil. In this strictly rural epidemic *Aedes aegypti* mosquitoes were not found but many other insects were present and the epidemiologic evidence pointed to some other vector or vectors. Since that time more than twenty similar outbreaks have been observed in various parts of South America which have demonstrated that man is generally infected only while in contact with the forest or jungle. Household infections, in fact, have been uncommon except when the house stands within the jungle. It has been shown, furthermore, that a number of Brazilian mosquitoes other than *Aedes aegypti* can become infected under laboratory conditions, but successful transmission by bite has been obtained with only three species: *Aedes scapularis*, *Aedes fluviatilis* and *Haemagogus capricorni*. The 1938 outbreak of jungle yellow fever in the state of Rio de Janeiro, Brazil, afforded an opportunity actually to demonstrate the presence of yellow fever virus in mosquitoes caught in the jungle.² More than 24,000 mosquitoes were sent in over a period of eleven weeks. Positive results with monkeys and mouse protection tests were obtained with *Aedes leucocelaenus*, *Haema-*

gogus capricorni and one or more as yet unidentified species of sabethine mosquitoes. The evidence presented thus incriminates two species of forest inhabiting mosquitoes, *Aedes leucocelaenus* and *Haemagogus capricorni*, as natural vectors of yellow fever and indicates that one or more species of sabethine mosquitoes may harbor the virus of the disease, although the latter have not been definitely implicated in actual transmission. Thus, while there is little reason to believe that *Aedes aegypti* is not usually the most important vector of yellow fever, the identification of other natural mosquito vectors has enormously complicated the problem of yellow fever control.

DOCTORS AND LAWYERS

Editorially the *San Francisco Chronicle* said recently:

The State Board of Medical Examiners announces that 172 of 174 applicants had passed the examination for physicians and surgeons recently held in San Francisco. Only two fell short of the high grade of 75 per cent required, and these two would doubtless have met any less stringent standard. On the same day, eleven out of fourteen met the requirements for the much more limited art of chiropody.

There has never been an examination for admission to the bar of California, since the present examination system was established, on which anything approaching this proportion of success was reached. It would be a rare examination which even half of the applicants passed.

And this is not because the standards for lawyers are higher than those for physicians, or the examinations more difficult. The exact contrary is the case. If the preliminary training of aspirants to the bar were uniformly as high as that in medicine, most of the candidates would pass, too. In fact, nearly all of those who have this training do pass.

The difference is that there are now no medical schools but class A schools; they admit none but highly selected university graduates, and they permit only those to remain in medical school who show the necessary ability and diligence. Naturally, the survivors of this process pass the state examinations also, with few or no exceptions.

If the law is ever to be in fact what it has always been in name, a "learned" profession, the same standards of preparation will have to be required of aspirants to it. The question still remains whether the law should be a learned profession. Curiously enough, there are two opinions in this. There is only one, as to medicine.

This comment indicates and emphasizes the necessity for an objective, unbiased grading of professional schools. A single state board could not possibly undertake the examination and rating of such schools, for the boards have neither funds nor trained personnel. Associations of professional schools could not assume the responsibility for self appraisal because the schools cannot escape being motivated by self interest. In medicine the medical profession itself, through the Council on Medical Education and Hospitals, has provided an independent yet dependable classification which has won the support of public opinion and thereby gained all but universal acceptance. In the field of legal education there has been much improvement as a result of the efforts of the American Bar Association, but a truly satisfactory standard will not be attained as long as the people themselves are undecided as to whether the law is, or is not, a learned profession.

1. Yellow Fever Studies, editorial, J. A. M. A. 105:1272 (Oct. 19) 1935.

2. Shannon, R. C.; Whitman, Loring, and Franca, Mario: Yellow Fever Virus in Jungle Mosquitoes, *Science* 88:110 (July 29) 1938.

ORGANIZATION SECTION

AMERICAN MEDICAL ASSOCIATION STUDY OF MEDICAL CARE

Walker County, Alabama

Proceeding with the plan to present some of the reports from county medical societies throughout the country, the information on the Summary Sheet and the accompanying comments for Walker County, Ala., are given.

Walker County has a population of 65,000, of which a little over 5,000 live in the city of Jasper. Forty-three forms were sent out to physicians and dentists, of which seventeen were returned. In addition to physicians and dentists two hospitals located in the county, the nurses' organization and the health department all contributed information to the Survey, as did one additional organization.

There are thirty-five physicians in active practice, and the greatest distance that the nearest physician would have to travel to reach persons in the area was 15 miles. There were four full-time and three part-time nurses, twelve pharmacists and two hospitals, both of which were general hospitals. There were twenty private rooms, twenty semiprivate rooms and sixty-four wards in the hospitals. During 1937 22.5 per cent of the private rooms were occupied, 10 per cent of the semiprivate rooms and 30 per cent of the ward beds. The charges in the hospitals varied from \$5 to \$6 a day for accommodations in private rooms, \$3.50 in semiprivate rooms and from \$2 to \$2.50 in wards.

Five outpatient departments or clinics were operated, one by a hospital and four by health departments. In addition, the Kiwanis Club provided for between eighty and 100 tonsillectomies in a special clinic.

All medical services in the schools in the neighborhood are supervised by the health department with one exception, where another agency is responsible for such supervision. Medical service in the schools is confined almost exclusively to examinations.

There are seventeen plant arrangements for medical service. Practically all the coal mines and the lumber operators have contract schemes providing ordinary medical care at a cost of from \$1 to \$1.50 a month and hospitalization for the entire family for an equal additional sum. This covers about 13,000 persons.

The seventeen physicians who returned the forms reported that they had given free services to 1,282 persons during 1937, and the dentists reported seventy-five who had been given dental care without charge. In addition, 487 hours was given by physicians to the care of free ambulatory patients in outpatient departments, dispensaries or clinics. Of the hospital patients, 1,727 were classified as pay and part pay, 394 as public charges and sixteen as free patients. The public charges received 2,670 days of hospital care and the free patients 161 days. Visits by 189 patients to outpatient departments, clinics and dispensaries totaled 252 during 1937. Pharmacists reported that they had compounded 387 prescriptions for which no charge was made and 600 at cost or reduced fees.

The ability or inability of patients to pay was determined by the Department of Public Welfare, and the funds for the medical care of the indigent were provided by the city or county.

No patients who needed hospital care were denied admission or turned away from outpatient departments, and the nurses reported that there was no one in need of medical service which it was found impossible to secure. The Health Department, however, reported that 150 persons requested medical care which could not be furnished owing to lack of funds. In reply to the question as to the "Total number of persons, during 1937 . . . who were unable to obtain either medical, dental, nursing or hospital care" it was stated that "No definite number reported by any physician, but there were probably several hundred."

One per cent of the births were unattended by a physician or midwife, and 98 per cent of those born alive were immunized against diphtheria. Forty-two per cent of the obstetric patients waited until after the third month before consulting a physician.

There was a birth rate of 25.5, a death rate of 7.4 and a maternal mortality rate of 6 per thousand. There was a diphtheria morbidity rate of 2.3 per thousand and an infant mortality rate of 35 per thousand. Three of five pharmacists reported that there was a decrease between 1936 and 1937 in the number of sales of home remedies or "patent" or proprietary remedies as compared with physicians' prescriptions.

Some of the comments which accompany the report were as follows:

It is clearly the opinion of all the medical and dental groups that there should be no complete federal or state control of the practice of medicine as a whole. Many express the opinion that there should be some form of government aid for the medical care to those who are already on the relief agency rolls and being furnished money for food and clothing. The majority opinion seems that whatever aid is offered should be furnished through the county units with the plan to be cooperative between the department of public welfare and the county medical society. Further opinion is advanced that the state government should offer some plan of hospitalization for the indigent in the private hospitals of the state, rather than in a large state charity hospital or hospitals.

(Comment: A hospitalization plan of this type would place many of the indigent who need medical care in the small community hospitals of the state where doctors serving on the staff could furnish medical and surgical attention free of charge and with but little expense to themselves.)

Believe medical society should have a fund which should be administered by the society to needy as approved by the Department of Public Welfare.

A setup should be made so that a person who is indigent could have medical care and medicine on the recommendation of the welfare worker and physician. The pharmacist and physician both should have their regular fee.

All coal mines and most lumber operations in this county have a contract physician. With the exception of one company employing 450 men, each employee contributes \$0.75 or \$1 for a single man, with an additional \$0.50 for the family and dependents. This covers ordinary medical care and medicines such as aspirin, quinine, cathartics, cold mixtures, and like inexpensive medicines.

The one exception does not make the men contribute, but no medicine is furnished and calls are not made more than 2 miles from the office.

At some of the mines \$1 per worker is paid to the hospital and ward service, operation and hospitalization are furnished. This includes x-ray. Does not include serums, vaccines, etc. Includes family.

One mine has mutual benefit run by U. M. W. A. \$1.50 per month, free choice of physician, limited choice of hospital. Does not include cancer, t. b., breaking law; maternity (hospital only in emergency operative cases). Also takes care of burial.

One mine has same setup but at less rate and is always behind. Seventy-five per month.

Alabama group hospitalization also operates in area.

Prowers, Kiowa and Baca Counties, Colorado

The return of Summary Sheets from various county medical societies which have completed their phase of the work in the Study of Medical Care makes it possible to give short reports by counties based on their recorded data. The following information and comments are taken from the Summary Sheets and attached comments returned by the Prowers County Medical Society.

Prowers County Medical Society includes Prowers, Kiowa and Baca Counties, which are all located in the southeastern corner of Colorado. The three counties combined have an area of 5,980 square miles and a population of 23,700. Practically the entire population is engaged in farming except for the 4,233 persons in Lamar, the county seat of Prowers County, and the people in the smaller towns scattered throughout the counties.

In 1937 there were seventeen physicians in active practice, six dentists, two full time private nurses, one part time private nurse, two full time public health nurses and four pharmacists. The greatest distance the nearest physician would have to travel to reach persons in this area was 35 miles. There is only one general hospital, located at Lamar, and it has a total of forty-one beds.

Forms were sent to twenty-two physicians and dentists, and nine were returned; the hospital did not return its form, and only one nurse returned a form. Reports were received from one health department, three relief agencies, six schools, four pharmacists, and the Red Cross and American Legion. Two private agencies and one governmental agency arrange for or provide medical services. All three of them provide hospitalization, drugs, eye glasses and surgical appliances, and one provides care in the physician's or dentist's office and one in the home. Of the six schools below college which answered the forms, three have only inspection and three give examinations, but none of them provide any medical treatment. There are no colleges in this area. Medical services for special groups are provided by the State Antituberculosis Association and the State Aid to Crippled Children.

The physicians who reported estimated that they had provided 2,130 persons with free medical care and the dentists 235 persons with free dental care. No patients

were referred to the hospital for free care and only thirteen made direct application for such care. The total number of pay and part pay patients in the hospital in 1937 was 399, public charges 243, free thirteen. The total patient days of hospital care was 5,032. Of this, pay or part pay patients received 2,564 days, public charges 2,349 days, free patients 119 days. The pharmacists compounded fifty free prescriptions and 100 or more at cost or reduced prices.

The relief agencies provide medical care for the indigent. Welfare workers determine the indigence of the persons applying for such care. Funds to pay for medical care come from the county, state and federal governments for the county relief agencies. Two private philanthropic agencies, the Red Cross and the American Legion, provide funds for some medical care also.

The report states that no patient in need of hospital care failed to receive such care. The nurse reported that no person visited by her was not receiving medical care. Two thousand persons made requests for medical care from the health departments and received it in every case. The welfare and relief agencies reported that medical care was furnished to all persons needing it. However, there were 657 pupils in the schools who needed medical care and of these 238 did not receive it because of financial reasons or indifference.

All the physicians who took part in the study were active in performing preventive medical services in private practice as well as for the public health departments. Sixty per cent of the children who entered school for the first time in 1937 were successfully vaccinated against smallpox, but very few of the children born in 1937 were immunized against diphtheria.

With regard to the number of sales of medicine on physicians' prescriptions for the year 1937 as compared to 1936 in relation to the number of sales of home remedies or "patent" or proprietary remedies, three pharmacists reported an increase and one reported a decrease in sales of medicine on physicians' prescriptions.

In general the comments which accompanied the Summary Sheet express the opinion that no person who needed and requested medical care failed to obtain such care but that medical care should be made more easily available to people in the rural areas. Some of the comments were as follows:

FROM SCHOOLS

1. No adequate program of health is functioning in our schools.

4. I feel that our Health Program is not sufficient. In many cases the children needing help are financially unable to see a doctor or dentist. I believe the school or county should have a doctor or dentist to take care of children when they are in need.

FROM COUNTY NURSE

At the present time our local doctors are ably caring for the indigent sick, through local arrangements with the County and Bureau of Public Welfare and their own contributions of their time, service and supplies used in the care of the indigent. In the dry land section of our county are 672 dry land farms. These people live some as far as 35 miles from a doctor and hospital. Many are very poor and do not seek medical care until a late date. These ten doctors in the county supply an area covering 1,043,200 acres. Six of these doctors are located in the city of Lamar; the other four, some of which live in small towns, reside about 25 miles from Lamar. The need is to reach the expectant

mother, the mother with the infant and small children, with nutritional problems. Sanitation: the care for tuberculosis patients and the contacts, the need for corrections of physical defects in the children is ever present, and keeps a public health nurse ever anxious for adequate medical care.

FROM WELFARE DEPARTMENTS

The need for medical care in this county seems to be more acute than in some neighboring counties. This may be due to several causes such as continued extreme drought and dust, possible former malnutrition of children, etc. This is evidenced by the fact that approximately 30 per cent of all relief costs in this county are used for medical and hospitalization purposes. We believe that a close cooperation between the county medical society, the department of public welfare and the state department of public health is necessary in order to somewhere near adequately care for the health of indigent residents. We have

observed that, in the local area where county physicians are changed every two months, unsatisfactory situations occasionally develop. We would recommend consideration of some plan which would provide that indigent medical patients could have their choice of physicians.

FROM AMERICAN LEGION

Medical care well supplied by present methods.

FROM RED CROSS

We believe all needs are well taken care of under present arrangements.

FROM PHARMACISTS

I believe there should be provisions made for county or districts of two or three counties, clinics available to indigents and people of low incomes.

I believe the present county relief is satisfactory.

WOMAN'S AUXILIARY

Colorado

The auxiliary to the State Medical Society of Colorado held its annual meeting at the Stanley Hotel, Estes Park, September 8-10. Frederic H. Douglas, curator of Indian art, Denver Art Museum, was speaker at the dinner on Thursday evening September 8. Dr. John W. Ames of Denver was speaker at the joint banquet and dance of the medical society and auxiliary September 10.

The auxiliary to the Denver Medical Society held its annual theater party at Elitch's June 26 for the purpose of raising funds for the work of the auxiliary. The net proceeds were \$465.

Indiana

The auxiliary to the Indiana State Medical Association held its annual meeting at the Murat Temple, Indianapolis, October 4-6. Dr. Norman M. Beatty, chairman of the Committee on Public Policy and Legislation of the Indiana State Medical Association, was the speaker at the annual auxiliary breakfast October 5.

The Indiana auxiliary published its first edition of the *Hoosier News-Letter* about October 1. Mrs. W. F. Hughes, 4025 North Meridian Street, Indianapolis, is its editor.

Kentucky

The sixteenth annual meeting of the auxiliary to the Kentucky State Medical Association was held in Louisville October 3-6. Speakers at the annual luncheon were Mrs. Charles C. Tomlinson, president of the Auxiliary to the American Medical Association, Mrs. Luther Bach, president of the Auxiliary to the Southern Medical Association and Drs. Horace G. Reynolds, William E. Gardner, Virgil Kinnaid, Arthur T. McCormack, and Van A. Stille. During the convention a study class was held on Eye Conservation and Prevention of Blindness.

Louisiana

Mrs. Frederick G. Ellis of Shreveport is president and Mrs. S. M. Blackshear of New Orleans is president-elect to the auxiliary to the Louisiana State Medical Society for 1938-1939.

The Shreveport Medical Association entertained its auxiliary with a dinner at the Shrine Club at Cross Lake August 9. Drs. Paul D. Abramson and Robert Lucas were speakers. Special guests were Mayor and Mrs. Sam S. Caldwell. More than eighty physicians and their wives attended the meeting.

Michigan

During the past year the Battle Creek auxiliary provided maternity kits for about 500 indigent mothers and is now making plans to furnish a room in the new community hospital.

The auxiliary to the Kalamazoo Medical Society provided a Fairchild hearing aid for the use of children in the hard of hearing department in the public schools. The auxiliary has assisted the Grand Rapids Medical Society in providing a benevolent fund to be used for members and their dependents in distress.

Oregon

The Multnomah County auxiliary enrolled thirty-three new members since the beginning of the fiscal year up to August 1938. Members of this auxiliary have knitted sweaters and purchased four dozen sun suits for the children at the Albertina Kerr Nursery. This auxiliary has made eleven loans this year to students in the junior and senior years at the University of Oregon Medical School, all made on recommendations of members of the faculty. The auxiliary sponsored a "Doctor's Hobby Show" for the last week in September, and as early as August forty-six doctors had requested space for exhibits. —The Benton County auxiliary has collected instruments and equipment which belonged to various pioneer physicians and placed them in the Oregon State College Museum. This county auxiliary has also placed *Hygieia* in many of the rural schools. —The Coos-Curry Counties Woman's Auxiliary has adopted the County Farm as the project to which their interest is to be devoted in providing entertainment for the inmates. —Members of the Klamath-Lake County auxiliary, have provided thirty quarts of canned fruit and several dozen glasses of jelly to the WPA nursery school. During the Nurses' state convention this auxiliary held a tea for the nurses at the home of Mrs. E. D. Johnson.

Virginia

The sixteenth annual meeting of the auxiliary to the Medical Society of Virginia was held at Hotel Danville, Danville, October 4-6. Mrs. James B. Stone of Richmond is president and Mrs. Hawes Campbell of Venter is president-elect. Speakers at the annual luncheon were Drs. G. F. Simpson, president, and Alex F. Robertson, president-elect, of the Medical Society of Virginia, P. W. Miles, president of the Danville-Pittsylvania County Medical Society and P. St. L. Moncure, chairman of the advisory council to the auxiliary.

The auxiliary to the Norfolk County Medical Society realized \$377.39 from three entertainments at the Norfolk Yacht and Country Club during the year. The proceeds were given to a patient at the Tidewater Memorial Hospital and used for other philanthropic work.

Members of the auxiliary had charge of booths during the drive for funds for the American Society for the Control of Cancer. The auxiliary contributed ten cents from its treasury for each active member to the Jane Todd Crawford Memorial.

The Accomac-Northampton auxiliary held a social meeting July 5 at the Accomac Country Club. Members of the medical societies of both counties and nurses from the Accomac-Northampton Hospital were guests of the auxiliary.

The auxiliary to the Williamsburg-James City County Medical Society held a program on health June 27 at the home of Mrs. W. L. L. Smoot. The importance of a yearly physical examination for every individual was emphasized.

Wisconsin

An auxiliary to the LaCrosse County Medical Society has recently been organized under the direction of Mrs. Eben J. Carey, state organization chairman.

MEDICAL ECONOMIC ABSTRACTS

COMPARISONS OF INFANT MORTALITY

Scientific comparisons of vital statistics from different nations are notoriously difficult. Differences in economic, climatic, racial and general social environment, as well as in statistical methods, are so great in quantity and diverse in quality as to make all conclusions based on such comparisons subject to a wide margin of error. Since constantly repeated comparisons of infant mortality disregard all these distorting elements, it may assist a fairer conclusion if an effort is made to eliminate some of the misleading factors.

The population of the United States is a mixture of nearly all races. Some of the most important racial ingredients have a high infant mortality in their native countries; nearly one tenth of the population is composed of Negroes—often with an infant death rate twice as high as that of the white population. Sectional differences in infant mortality rates are greater than in almost any other country. Comparisons of absolute rates at any given period exaggerate nearly all these errors more than comparisons of the rate of change in mortality. This is peculiarly significant when considering the effects of any efforts to reduce infant mortality. Comparisons of rate of change may be equally misleading unless the points of

parable in climate, racial characteristics and general social conditions with the European nations listed in table 1.

The large Negro population in some of these states tends to make this comparison unfavorable to the United States. However, standards of living average higher here than in some of the European nations listed.

No attempt is made to allow for errors in registration of either births or deaths, although these are often significant.¹

These figures would seem to indicate not only that in the states listed the rate was on the average lower in 1920 but that in spite of this handicap the death rate declined more rapidly in the United States than in Europe. At the present time the rate of infant mortality is lower in these sections of the United States than in those European nations in which conditions are most nearly comparable.

"INDEMNITY INSURANCE"

The House of Delegates of the American Medical Association at its recent special session approved "cash indemnity insurance" as a method of paying medical costs. Unthinking exponents of socialized medicine may endeavor to twist this approval into a reversal of policy. There are, however, basic differences in the most vital points of the two systems.

Practically no one—and certainly not the American Medical Association—has ever opposed the *payment of medical bills through insurance*. The medical profession has objected most strenuously and continues to object to the *compulsory wholesale purchase and retailing* of medical service to patients by an insurance company, government agency, or any other organization or individual. This objection rests on the proof afforded by vital statistics that during this process of purchase and retailing the medical service is adulterated by politics and depreciated by administrators until it loses much of its value as a protection of the public against disease and death.

Sickness insurance in most countries arose out of systems of contract practice, the administrators of which wished to keep control of the medical service. Politicians were quick to see that service benefits could be sold to voters unable to judge their value for greater political assets than could cash benefits. In the most commonly advocated plans of voluntary and compulsory sickness insurance, premiums are collected in cash and then transformed within the insurance administration into service benefits for the insured. All other systems of insurance collect premiums and pay benefits in the medium of exchange. The two sides of the balance sheet are then written in the same units. It is much more difficult to tamper with the book-keeping for political purposes or to deceive the sick as to the benefits received than in systems in which receipts are counted in cash and benefits are delivered in an unmeasurable service. Indemnity insurance collects the premiums in cash and pays cash to the insured on a definite scale in accordance with the economic losses suffered from sickness.

There would be fewer complications and far less red tape in such an indemnity system than in one with service benefits. Free choice of physician would be automatic. Restrictions on prescribing and other phases of treatment would be unnecessary, as there would be no need to deceive the patient as to the quality and extent of the service he was receiving.

This is not a proposal for an untried experiment. Such a system is in almost universal use by commercial insurance companies. It has been introduced with success into some industrial plans. It is the plan on which old-age, unemployment, and all other forms of social insurance are conducted. There is a decided trend in this direction in even the compulsory systems, as shown by certain features of the French and Swedish sickness insurance plans; both of these, however, are still more or less hybrids of the indemnity and service systems. They retain so many of the evils of the latter, aside from their governmental, compulsory feature, that they cannot be offered as patterns to follow.

TABLE 1.—*Infant Mortality*
(Deaths of children under one year per thousand live births)

Countries	1920	1935*	Per Cent of Decline
Austria	157	100	36
Belgium†	104	85	18
Canada‡	102‡	71	30
Denmark	90	71	21
England and Wales	80	57	29
France	99	69	30
Germany	130	68	48
Italy§	127	101	20
Netherlands	73	40	45
Scotland	92	77	16
Sweden	63	47	25
Switzerland	84	48	43
United States§	86	56	35

* Preliminary figures.

† Previous to 1934, infants born alive but who died almost immediately after birth are not included.

‡ Registration population, slightly smaller than the total population.

§ Rate for 1920 not given; 102 is the rate shown for 1921.

¶ From 1921, the rates relate to the present area.

§ Birth registration area (59.8 per cent of total population in 1920 and 100 per cent since 1933).

TABLE 2.—*Infant Mortality*
(Deaths, exclusive of stillbirths, under 1 year of age per thousand live births)

State	1920	1935	Per Cent of Decline
Iowa	54.9*	47.1	14
Massachusetts	90.9	48.3	47
Minnesota	66.4	44.7	33
Nebraska	64.2	41.2	36
New Hampshire	88.0	53.9	39
New Jersey	74.1†	46.2	38
New York	86.3	48.0	44
Oregon	61.8	41.2	33
Rhode Island	92.7‡	47.2	49
Washington	66.4	45.2	32
Wisconsin	76.5	46.0	40

* Rate for 1924, first year Iowa was included in birth registration area.

† Rate for 1921, first year New Jersey was included in birth registration area.

‡ Rate for 1921, Rhode Island was dropped from registration area in 1919 and readmitted in 1921.

departure also are compared. The curve of a declining mortality rate always flattens out rapidly and approaches a level which it is extremely hard to lower further.

It is not claimed that the statistics given herewith provide perfect comparisons but only that they eliminate some of the more flagrant and frequent errors. Table 1 is taken from the 1937 issue of the Epidemiological Report of the League of Nations, pages 67 and 68. Unless otherwise noted, it compares the infant mortality rate in various nations in 1920 with that in 1935.

The figures in table 2 are taken from Vital Statistics—Special Reports Vol. 5, No. 17, page 47, Bureau of the Census, March 1, 1938. The table includes states most nearly com-

1. Woodbury, Robert M.: Infant Mortality in the United States, *Annals of the American Academy of Political and Social Science* 188: 94 (Nov.) 1936.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

CALIFORNIA

Society News.—The San Diego County Medical Society was addressed September 13, by Arthur I. Kendall, Ph.D., Chicago, on "Virus Diseases"; Dr. Philip E. C. Manson-Bahr, London School of Tropical Medicine, addressed the society August 17.

Institute on Health Education.—The Los Angeles Tuberculosis and Health Association recently sponsored an institute on community health education on the Los Angeles campus of the University of California. Ira V. Hiscock, C.P.H., professor of public health, Yale University School of Medicine, New Haven, Conn., conducted the program, which covered all phases of health education. The value of radio, motion pictures, newspapers, exhibits and group contacts was considered.

FLORIDA

Miami Visitors from Yellow Fever Foci Must Report to Health Authorities.—Since the flying time to Miami from actual or potential foci of yellow fever in South America has been shortened recently, the danger has increased of bringing passengers whose arrival, timed from the date of possible exposure, falls within the incubation period of the disease. To prevent introduction of the disease, Dr. George N. MacDonell, director of public health, issued an order July 1 requiring all such passengers who have within six days previous to their arrival been in any city, town or area which the U. S. Public Health Service has declared to be a focus, to report immediately to the health department. The visitors must remain under surveillance of the health department until six days from the time they departed from the danger zone in South America. If any febrile condition develops, the health department must be notified immediately. If the visitor should leave Miami before the six days has elapsed, he must report to the director of health and furnish information as to his movements. The order does not apply to travelers leaving the city immediately on arrival or to those who can show certificates of immunity to yellow fever.

GEORGIA

Society News.—A symposium on diseases of the biliary system was presented before the Fulton County Medical Society in Atlanta September 1 by Drs. Jean George Bachmann, Allen H. Bunce, James J. Clark and Daniel C. Elkin. Dr. Edward L. Graydon opened the meeting with "a few minutes of magic" and Dr. Frank K. Boland presided. Dr. Emmett D. Colvin presented a paper before the society in Atlanta September 15 entitled "Behavior of the Basal Metabolism in the Course of Developing Toxemia of Pregnancy: Correlation with Cholesterol, Placental Infarcts and Retinal Examination."

ILLINOIS

Meeting Dates Changed.—The Illinois State Medical Society has changed the date of its 1939 meeting from May 16-18 to May 2-4 to avoid conflict with the annual session of the American Medical Association in St. Louis May 15-19.

Society News.—At the second annual meeting of the Illinois Association for the Crippled in Chicago, September 15, Paul H. King, president, International Society for Crippled Children, spoke; John A. Lapp, LL.D., Chicago, discussed "The Value of a State Program for the Crippled," and Dr. Edward L. Compere, "The Program in Illinois." There was also a symposium on education, vocational training, guidance and employment. Dr. Compere was chosen president of the Illinois association at this meeting.—Drs. Clifford G. Grulee, Evanston, and William J. Dieckmann, Chicago, addressed the Knox and Warren county medical societies in Galesburg September 22 on "Care of the Premature Infant" and "Forceps Delivery" respectively.—The Adams County Medical Society was addressed September 12 by Dr. Ross A. Woolsey, St. Louis, on "Inguinal Hernia."—Dr. Ford K. Hick, Chicago, addressed the Peoria City Medical Society, September 20, on "Emotional Factors in Mental Hygiene."

Chicago

Personal.—Dr. Martha Wilson MacDonald, who has been in charge of the children's division of the department of psychiatry at Michael Reese Hospital for several years, has been appointed director of a new child guidance clinic in New Orleans. The new clinic has been made possible by a contribution from Mr. Samuel Zemurray, New Orleans, managing director of the United Fruit Company.—Mr. Paul Fesler, superintendent of Wesley Memorial Hospital since 1932, has resigned to become a consultant in hospital administration and construction.

Program on Sulfanilamide.—The Chicago Medical Society will hear a program on sulfanilamide at its meeting October 19. The speakers will be Paul Nicholas Leech, Ph.D., secretary of the Council on Pharmacy and Chemistry of the American Medical Association, on "Sulfanilamide, the Drug"; Dr. Eugene M. K. Geiling, "How Sulfanilamide Acts"; Dr. John S. Lockwood, Philadelphia, "The Clinical Status," and Dr. Paul R. Cannon, "Pathology." Mr. Walter G. Campbell, chief of the Food and Drug Administration, U. S. Department of Agriculture, Washington, D. C., will lead the discussion, and the following physicians will speak on the value of the drug: Drs. Joseph L. Baer, in obstetrics; Russell D. Herrold, urology; Julius H. Hess, pediatrics, and Italo F. Volini, internal medicine.

INDIANA

New Hospital for Tuberculosis.—Governor Townsend has appointed a committee to select a site for the construction of a tuberculosis hospital at some southern point in Indiana to cost \$650,000, 45 per cent of which will be financed by the PWA. Members of the commission include Arthur H. Sapp, Huntington, chairman; Thomas O'Mara, Terre Haute, vice chairman; Murray A. Auerbach, Indianapolis, secretary of the Indiana Tuberculosis Association, secretary; Lemuel A. Pittenger, president of the Ball State Teachers' College at Muncie, and Dr. Verne K. Harvey, Indianapolis, secretary of the state board of health.

Society News.—Dr. Ernest Perry McCullagh, Cleveland, addressed the Muncie Academy of Medicine September 13 on "Some Common Problems in Endocrine Therapy."—Dr. George S. Bond, Indianapolis, addressed the Carroll County Medical Society, Camden, September 8 on coronary artery disease.—Dr. Pierce MacKenzie, Evansville, addressed the Gibson County Medical Society, Princeton, September 12 on "The Three Stages of Labor, with Special Reference to Pain Relieving Preparations."—At a meeting of the Tippecanoe County Medical Society, Lafayette, September 13 Dr. Willis D. Gatch, Indianapolis, spoke on "Management of Wounds."—Dr. Carl J. Langenbahn, South Bend, addressed the Marshall County Medical Society, Plymouth, September 6 on "Chronic Gonorrhea in the Male."—Dr. Wayne R. Glock, Fort Wayne, addressed the Whitley County Medical Society, Columbia City, September 13 on "Backache."

LOUISIANA

Personal.—Dr. John Signorelli has been appointed medical director of the Orleans Parish School Board, succeeding the late Dr. Frederick L. Fenno.—Dr. Urban Maes, professor and head of the department of surgery, Louisiana State University Medical Center, New Orleans, received the honorary degree of doctor of science at the university's graduating exercises in Baton Rouge August 2.—Dr. William J. Rein, Pineville, has been appointed superintendent of the State Colony and Training School, Alexandria, it is reported. He will succeed Dr. Eugene M. Robards Jr., who resigned to devote his time to private practice.—Dr. Benjamin O. Morrison, Abbeville, has been appointed health officer of Acadia Parish.

MARYLAND

Semiannual Meeting of Medical Faculty.—The Medical and Chirurgial Faculty of the State of Maryland will hold its semiannual meeting at Chestertown October 12 with headquarters at the Armory. Dr. Frank B. Hines, Chestertown, president of the faculty, will give the address of welcome and Dr. Alexander Colclough Dick, the response. Dr. Alexander Randall, Philadelphia, will address the general meeting on "Diagnosis and Therapeutic Management of Early Obstructive Uropathies." A tea will follow the session.

MICHIGAN

Obstetrical Consultant Service.—Dr. Clair Folsome, instructor in obstetrics and gynecology, University of Michigan Medical School, Ann Arbor, has been appointed in charge of a newly created field consultant service in obstetrics recently inaugurated by the bureau of maternal and child health, state department of health. Dr. Folsome will cooperate with the maternal health committees of the county and district medical societies; his services are available to all physicians but at no time will he replace physicians who usually assist at deliveries, the state medical journal reports. The service may be obtained by any county medical society on request.

State Medical Election.—Dr. Burton R. Corbus, Grand Rapids, was chosen president-elect of the Michigan State Medical Society at its annual meeting in Detroit September 20 and Dr. Henry A. Luce, Detroit, was installed as president. Emeritus membership was conferred on Drs. John H. Jones, Dowagiac; George C. Hafford, Albion; Archibald B. Thompson, Grand Rapids; John W. Handy, Flint; Henry G. Berry, Mount Clemens; Ervin D. Brooks, Kalamazoo; Fred W. Freeman, Saginaw, and Joseph A. Crowell, Iron Mountain. The house of delegates of the society by unanimous vote approved the action of the House of Delegates of the American Medical Association at the recent special session in Chicago. The 1939 annual meeting will be held in Grand Rapids.

Certification in Graduate Education.—The Michigan State Medical Society held its first annual convocation for certification in graduate education in Detroit September 20 during its annual meeting. This convocation was the first of its type and was established to certify those physicians who attended special sessions in graduate education for four years. Physicians completing the first term, as it is designated, were made "associate fellows in graduate education." Fellowship will be conferred on completion of a second term. More than 500 physicians received certificates at the first convocation. Physicians unable to participate in the extramural courses covered in the program may take advantage of the intramural courses offered at the University of Michigan Medical School, Ann Arbor, and Wayne University College of Medicine, Detroit. Dr. Henry A. Luce, Detroit, presided at the convocation. Dr. James D. Bruce, in charge of graduate education at the state university, discussed "The Challenge of Medical Service" and Dr. Morris Fishbein, Chicago, Editor of THE JOURNAL, "Social Aspects of Medical Care." Drs. Henry Cook, Flint, and L. Fernald Foster, Bay City, presented the certificates.

MISSISSIPPI

Society News.—Dr. Julius L. Levy, Clarksdale, addressed the Coahoma County Medical Society and the Clarksdale Hospital medical staff August 10 on "Polydactylism."—Drs. Augustus Street and Willard H. Parsons, Vicksburg, addressed the Issaquena-Sharkey-Warren Counties Medical Society, Vicksburg, September 13, on "Surgical Diseases of the Gastro-intestinal Tract."

MISSOURI

Society News.—Drs. Lawrence Schlenker and John M. McCaughan addressed the St. Louis Medical Society September 27 on "Prontosil in Pyopneumothorax" and "Posterior Gastrojejunostomy." Speakers at a meeting of the society September 20 were Dr. Carl F. Vohs on the special session of the House of Delegates of the American Medical Association and Rev. Alphonsc M. Schwitalla, Ph.D., on the National Health Conference.

Dr. Goodwin Becomes Secretary-Editor Emeritus.—Dr. Edward J. Goodwin, for twenty-eight years secretary-editor of the Missouri State Medical Association, has retired with the title emeritus, and will be succeeded by Mr. Elmer Bartelsmeyer, who has been assistant secretary for several years. Dr. Goodwin graduated at the Washington University Medical Department, St. Louis, in 1894. He had been in private practice for a little longer than a year when an accident he suffered on alighting from a street car resulted in a paraplegia that totally incapacitated him for three years and made the future practice of medicine impossible. In 1902 he became associate recording secretary and official reporter of the state medical association; in 1903 assistant secretary; associate editor in 1905; editor in 1906 and in 1910 secretary-editor. He served as a member of the House of Delegates of the American Medical Association from 1909 to 1918 inclusive and from 1925 to 1934 inclusive. He was associate editor of the *Interstate Medical Journal* from 1903 to 1910, publishing the book "Medicine in Missouri" in 1905.

NEW JERSEY

Society News.—A symposium on diabetes mellitus will be presented before the section on medicine and pediatrics of the Academy of Medicine of Northern New Jersey, Newark, October 11, by Drs. Benjamin I. Saslow, Stuart Z. Hawkes and Anthony Russell Sherman.—Dr. Robert A. Kilduffe, Atlantic City, addressed a joint meeting of the New York and New Jersey chapters of the Association of Military Surgeons of the United States in Newark September 29 on "Disease and Destiny."—Dr. Harold D. Harvey, New York, addressed the Bergen County Medical Society, Englewood, September 20, on "Use and Abuse of Sulfanilamide."

NEW YORK

Hospital News.—Dr. Frederick C. Smith, formerly medical director of the U. S. Marine Hospital, Norfolk, Va., has been appointed acting director of Grasslands Hospital, Valhalla. He succeeds Dr. Arthur R. Bowles, who had been acting director since the resignation of Dr. Claude W. Munger in May 1937.

Society News.—Dr. Arthur J. Geiger, New Haven, Conn., addressed the Dutchess County Medical Society, Poughkeepsie, September 14, on "Practical Use of the Electrocardiogram in the Diagnosis and Follow-Up of Coronary Thrombosis."—The fall meeting and outing of the Associated Physicians of Long Island was held at Long Beach, L. I., September 29, with the following speakers, all of Hempstead: Drs. David Edward Overton, on "Longitudinal Sinus Thrombosis"; George B. Grauger, "Conduct of Labor"; Algernon S. Warinner, "Thyroid Disease from the Surgical Standpoint," and Louis H. Bauer, "Coronary Thrombosis."—Speakers at a meeting of the Medical Society of the County of Albany, Albany, September 28, were Drs. James S. Lyons on "Pyuria—Its Clinical Significance"; Arthur F. Holding, "Treatment of Malignant Disease of the Larynx," and Emanuel Martin Freund, "Observations and Analysis of Recent Hearing Surveys."—The New York State Association of Public Health Laboratories will hold its midyear meeting November 4 at the state laboratory in Albany.

New York City

Blood Tests for Marriage Licenses.—An increase of 4,000 blood tests given to persons seeking marriage licenses in August over the number given in July was reported by the New York City Department of Health. In July, the first month in which the law was operative, 6,656 premarital blood tests were given and in August 10,862.

Conviction for Making Noise.—An employee of the Interborough Rapid Transit Company power house at 110 East Nineteenth Street was convicted September 23 of violating the antinoise ordinance. Residents of the Gramercy Park section complained of the noise of the substation's dynamo. The court found that the noise constituted a violation of the ordinance because the doors of the power house were open while the dynamos were in operation. The judge suspended sentence.

Health Registration of School Children.—Twenty-five hundred mothers of school children joined the city school and health authorities when schools opened in September in the first health registration of the pupils. Members of the United Parents Association, the Queens Borough Federation of Mothers Clubs and other civic groups aided in the clerical work and interviewing in more than 600 schools. The registration cards identified each child by sex, race and date of birth; gave the name of the family physician and noted whether the child had had diphtheria, measles, whooping cough or scarlet fever. Space was left for other information to be obtained from a medical examination. Mothers were urged to take their children to a private physician if they could afford to do so; if they could not afford private care a request for health department examination and diphtheria immunization, if necessary, might be signed at the bottom of the card. Parents and guardians received a statement from Dr. John L. Rice, commissioner of health, explaining that a health certificate is required of each pupil on entering school, that vaccination is required by law and that diphtheria immunization is equally important. Parents able to afford an examination fee received a card to be filled in by a private physician and were told to return it within ten days. About 40,000 children were registered, a task beyond the capacity of the teachers, nurses or any available clerical staff, it was said.

NORTH CAROLINA

Society News.—Drs. Wilburt C. Davison, Durham, and Oren Moore, Charlotte, addressed the Catawba Valley Medical Society, Newton, September 13, on "Kidney Diseases of Children" and "Management of Obstetrical Malpresentations" respectively.—The Buncombe County Medical Society held a hobby show in Asheville August 31 with twenty-one exhibitors and 600 visitors.—E. N. Lawrence, D.D.S., Raleigh, addressed the Johnston County Medical Society, Princeton, September 20, on orthodontic problems.

Medical Symposium at Duke Centennial.—Duke University, Durham, begins a celebration of its centennial year with a "Symposium on Medical Problems" to be held October 13-15 in Page Auditorium in the school of medicine. William Preston Few, LL.D., president of the university, will give the welcoming address. Dr. Wilburt C. Davison, dean of the medical school, will preside. The speakers on scientific topics will be:

- Dr. Allen W. Freeman, Baltimore, Public Health Developments in the South.
- Dr. George W. McCoy, New Orleans, Leprosy in the United States.
- Dr. George Hoyt Whipple, Rochester, N. Y., Anemia and the Building of Hemoglobin in the Body.
- Dr. William H. Schrell Jr., U. S. Public Health Service, Pellagra.
- Dr. Charles Franklin Craig, New Orleans, Amebiasis.
- Dr. Edward William Alton Ochsner, New Orleans, The Surgeon's Contribution to Treatment of Amebiasis.
- Dr. William G. MacCallum, Baltimore, Malaria.
- Dr. Arturo Lorenzo Carrion, San Juan, Puerto Rico, Rising Significance of Fungus Infections in Man.
- Dr. Albert M. Snell, Rochester, Minn., Tropical and Nontropical Sprue (Chronic Idiopathic Steatorrhea); Their Probable Interrelationship.

Thursday evening October 13 there will be a discussion of "The Future of American Medicine" by Dr. Morris Fishbein, Chicago, Editor of THE JOURNAL; John P. Peters, New Haven, Conn., and Mr. Henry L. Mencken, Baltimore. Dr. Milton J. Rosenau, professor of epidemiology, University of North Carolina School of Medicine, Chapel Hill, will preside at this meeting. The scholastic year 1938-1939 has been designated as a time for celebration of a century of development which has resulted in the Duke University of today. The college was first named Union Institute, then was a normal college, and later Trinity College, which continues as the undergraduate school for men in the university. A formal celebration of the anniversary will be held April 21-23, 1939.

OREGON

State Program for Care of Low-Wage Earners.—The house of delegates of the Oregon State Medical Society at its annual meeting in August adopted a program for medical care of low income groups. The delegates first established a bureau of medical economics, whose services are to be made available to the component societies in developing special plans for care of low wage industrial groups. Each component society is to be asked to indicate whether the problem of this group and of contract practice is such that a special plan is desirable. Then on request of any component society, representatives of the bureau and legal counsel will be sent to make a survey of the local situation and advise in local plans. Any plans developed are to be submitted to the executive committee of the council of the state medical society for review as to conformity to policies and ethical standards. The statement of the delegates emphasized the principle that each local plan should limit its activities to the jurisdiction of the medical society by which it is approved except in special cases. Among other duties laid on the bureau of medical economics, it will develop uniform by-laws for plans, draft schedules of rates to subscribers, install uniform accounting practices as far as feasible, and develop general policies for guidance of local organizations. The delegates agreed to cooperate with the Oregon Association of Hospitals in the development of a plan for hospital care on a prepayment basis.

PENNSYLVANIA

Graduate Seminar at Wilkes-Barre.—The Wilkes-Barre General Hospital presented its Fourth Annual Postgraduate Seminar September 15. Guest speakers were Drs. Rupert F. Carter, New York, on "Surgical Management of Cholecystitis"; John A. Kolmer, Philadelphia, "The Toxicity and Therapeutic Applications of Sulfanilamide," and Irving S. Wright, New York, "Peripheral Vascular Disease."

Personal.—Dr. Martha Edith MacBride-Dexter, Harrisburg, secretary of health of the Commonwealth of Pennsylvania, recently received from the governor a meritorious service medal in recognition of her work during the flood of 1936.

—Dr. James Reid Martin, assistant professor of orthopedic surgery, Jefferson Medical College, Philadelphia, has been appointed chief surgeon at the Elizabethtown Hospital for Crippled Children.

Society News.—Dr. Roy R. Snowden, Pittsburgh, addressed the Cambria County Medical Society, Johnstown, September 8, on "The Anemias."—Dr. Philip F. Williams, Philadelphia, addressed the Northampton County Medical Society at the Country Club of Northampton County September 16 on "Maternal Welfare."—Dr. Eurfryn Jones, Camp Hill, addressed the Dauphin County Medical Society, Harrisburg, September 6, on "Differential Diagnosis of Hynertthyroidism."—At a meeting of the Lycoming County Medical Society, Williamsport, September 9, the speakers were Drs. Frederic C. Lecner, Montoursville, on "Woldman Treatment of Peptic Ulcer"; Irvin T. Gilmore, Picture Rocks, "Chronic Ulcerative Colitis" and Chauncey L. Palmer, Pittsburgh, "Public Health Legislation."

Philadelphia

Bequests of Dr. de Schweinitz.—The University of Pennsylvania School of Medicine will eventually receive the bulk of the estate of the late Dr. George E. de Schweinitz to found a chair of ophthalmology. Except for one bequest of \$6,000, the estate of \$105,000 was left in trust for a sister of Dr. de Schweinitz. After her death \$5,000 will go to the College of Physicians of Philadelphia and the residue to the university. He also left his medical library to the College of Physicians. Dr. de Schweinitz died August 22.

Program of College of Physicians.—Drs. Homer F. Swift and Alfred E. Cohn, New York, will give the first lecture of the 1938-1939 season before the College of Physicians of Philadelphia October 12 on "Cardiac Diseases: Infectious and Noninfectious, Course and Consequences." Lectures for the coming months will be:

- Dr. Edward A. Strecker, Philadelphia, November 2, Should Psychoanalysis Be Purged?
- Dr. William K. Boyd, Toronto, December 7, Some Reasons for the Recent Increase in Bronchial Carcinoma.
- Dr. Walter Bauer, Boston, Jan. 4, 1939, Studies Pertaining to the Origin and Nature of Hypertrophic Arthritis.
- Dr. Cyril N. H. Long, New Haven, Conn., Feb. 1, 1939, Diabetes Mellitus in the Light of Our Present Knowledge of Metabolism.

TEXAS

Personal.—Dr. Bolivar J. Lloyd, medical director, U. S. Public Health Service, retired, Washington, D. C., has been appointed director of a recently organized health unit for Austin and Travis County. Dr. Benjamin M. Primer, recently health officer of Amarillo and Potter County, has been made assistant to Dr. Lloyd.—Dr. Robert L. Cherry, Kaufman, director of the district 3 health unit of the state department of health, has been appointed health officer of the Tyler-Smith County Health Unit to succeed Dr. Austin E. Hill, Tyler. Dr. Hill has been appointed director of communicable diseases, epidemiology and maternal and child health in the health department of Houston.

Society News.—Dr. Louis F. Knoepf, Beaumont, was chosen president of the Texas Tuberculosis Association at its recent meeting in El Paso. Dr. McIver Furman, Corpus Christi, is secretary.—Dr. Edward Stanley Peterman, Crowley, La., addressed the Jefferson County Medical Society, Beaumont, August 8, on "Goiter, with Special Emphasis on Hyperthyroidism."—Papers on nephritis were presented at a meeting of the Lubbock-Crosby Counties Medical Society, Lubbock, August 2, by Drs. Samuel C. Arnett Jr., Emerson M. Blake and Byron A. Jenkins, Lubbock.—Drs. Eutus P. Bunkley and Frederick E. Hudson, Stamford, addressed the Taylor-Jones Counties Medical Society, Abilene, July 12 on "Perforated Peptic Ulcer" and "Diseases of the Thyroid Gland and Other Disorders of Metabolism" respectively.

WASHINGTON

State Medical Election.—Dr. Warren B. Penney, Tacoma, was chosen president-elect of the Washington State Medical Association at the annual meeting at Bellingham August 31 and Dr. Harry E. Rhodhamel, Spokane, was installed as president. Dr. Vernon W. Spickard, Seattle, was reelected secretary. The next annual meeting will be held in Spokane.

King County Celebrates Golden Anniversary.—The King County Medical Society celebrated the fiftieth anniversary of its founding with a banquet at the Olympic Hotel, Seattle, September 24. Dr. Clarence W. Knudson, president of the society, gave a welcoming address and introduced the toastmaster.

Dr. Caspar W. Sharples. Honor guests were twelve of the first hundred members of the society; one of them, Dr. Lewis R. Dawson, was a charter member. Dr. Park Weed Willis, one of this group, unveiled a portrait of Dr. Gideon A. Weed, first president of the society. Dr. Clarence A. Smith, another of the early members, introduced the honor guests. A portrait of Dr. Smith, who has been editor of *Northwest Medicine* since that journal was established in 1903, was unveiled by his son, Rev. Dwight C. Smith, Bellingham. Dr. Morris Fishbein, Editor of THE JOURNAL, was the guest speaker on "American Medicine and the National Health Program." In further observance of the anniversary the society sponsored a health exposition in cooperation with the Washington State Medical Association and the Public Health League of Washington September 15-27 at the Masonic Temple. In addition, the society sponsored a medical supplement to the *Seattle Sunday Times* of August 21. Dr. Shelby Jared was chairman of the committee which selected material and scrutinized all advertising for the supplement. The *Times* also published an editorial tribute to the medical profession in the same issue, directing attention to the supplement.

WISCONSIN

Society News.—Drs. Arnold S. Jackson and Hugh P. Greeley, Madison, addressed the Oneida-Vilas Counties Medical Society, Rhinelander, August 4, on "Diseases of the Thyroid Gland—Their Diagnosis and Treatment" and "Hypertension and Heart Disease" respectively.

State Medical Election.—Dr. Raymond G. Arveson, Fred-eric, was chosen president-elect of the State Medical Society of Wisconsin at the annual meeting in Milwaukee September 14 and Dr. Albert E. Rector, Appleton, was installed as president. The 1939 session will be in Milwaukee.

GENERAL

Meeting of Record Librarians.—The tenth annual conference of the Association of Record Librarians of North America will be held in New York October 17-21.

Southern Psychiatrists to Meet.—The Southern Psychiatric Association will hold its annual meeting in Atlanta, Ga., October 10-11. Among the speakers will be Drs. Gregory Zilboorg, New York; George Sidney Sprague, White Plains, N. Y.; Walter E. Dandy, Baltimore; Winfred Overholser, Washington, D. C., and Raymond S. Crispell, Durham, N. C. Dr. George Percy Sprague, Lexington, Ky., is president of the association.

Magazine Office Disappears.—Physicians have reported to the American Medical Association that they subscribed to a magazine called "Medicine Today, Inc.," and received only one copy. Information from the Better Business Bureau in New York indicates that the magazine has moved from its address at 425 Fourth Avenue, New York, and left no forwarding address. One issue was received in the Library of the American Medical Association. It contained principally summaries of addresses delivered before New York medical societies and hospital staffs.

New Head of Carnegie Institution.—Vannevar Bush, D.Sc., vice president and dean of engineering, Massachusetts Institute of Technology, Cambridge, Mass., has been elected president of the Carnegie Institution of Washington to succeed John C. Merriam, LL.D., who was president for seventeen years. Among the branches of the institution are the Station for Experimental Evolution at Cold Spring Harbor, N. Y., the Biological Station in the Dry Tortugas Islands in the Gulf of Mexico, the Nutrition Laboratory in Boston and the Laboratory of Embryology in Baltimore.

Bacteriology Prize Awarded to Dr. Syverton.—The Eli Lilly prize in bacteriology and immunology, consisting of \$1,000 and a medal, was awarded to Dr. Jerome T. Syverton, assistant professor of bacteriology at the University of Rochester (N. Y.), at the annual meeting of the Society of American Bacteriologists in San Francisco August 31. The award was made in recognition of Dr. Syverton's work on the filtrable viruses, especially on the transmission of the virus of equine encephalomyelitis and on simultaneous infection with several viruses. Dr. Syverton is 31 years old and a graduate of Harvard University Medical School, Boston, class of 1931.

Hospital Journal Twenty-Five Years Old.—*Modern Hospital* marked the twenty-fifth anniversary of its founding with a special issue in September. Among the features were an article by Dr. Sigismund S. Goldwater, hospital commis-

sioner of New York, who contributed to the first issue; articles and pictures contrasting hospital practices in 1913 and 1938; a history of the magazine, and a reproduction of eight pages from the first issue. The magazine was first published in St. Louis, with Dr. Otho F. Ball, Chicago, as publisher and Dr. John A. Hornsby as editor. Dr. Ball is the present president of the publishing firm, now in Chicago; Dr. Hornsby resigned shortly after the World War and is now living in Washington, D. C. Dr. Joseph C. Doane, Philadelphia, is editor.

Scholarships Available at Forlanini Institute.—The Italian ambassador at Washington, D. C., has offered two scholarships for a graduate course in tuberculosis to be given from January 15 to April 15 at the Carlo Forlanini Institute in Rome. Applications must be sent to the Surgeon General, U. S. Public Health Service, Washington, D. C., before October 25. The candidates should have been graduated from medical school for at least three years and should have practiced in institutions specializing in treatment of tuberculosis. The physicians chosen will be exempt from registration and tuition fees and will receive 50 per cent discount for travel on Italian state railroads. The course will cover the following aspects: pathogenesis, biologic factors, clinical forms, histology and histogenesis, pathologic anatomy, collapse therapy technic, pleural complications and extrapulmonary tuberculosis. The Forlanini institute has 1,400 beds and has recently begun construction of a new hospital for nontuberculous diseases of the lungs. It is under the direction of Dr. Eugenio Morelli, a former pupil of Dr. Forlanini.

American College of Surgeons.—The twenty-eighth annual clinical congress of the American College of Surgeons will be held in New York October 17-21 with headquarters at the Waldorf-Astoria and under the presidency of Dr. Howard C. Naffziger, San Francisco. Clinics will be held each day in numerous hospitals in New York, except Wednesday, when the programs will be presented in Brooklyn hospitals. Afternoon sessions will be devoted to symposiums on cancer, surgical procedures on the handicapped patient, industrial medicine and traumatic surgery, fractures, obstetrics and gynecology and urologic infections. Among speakers at evening sessions will be:

Prof. Hans Finsterer, Vienna, Results with Repeated Stomach Operations.

Dr. William H. Ogilvie, London, The Radical Operation for Cancer of the Stomach.

Dr. Franklin G. Ebaugh, Denver, The Psychiatrist in Relation to Surgery.

Dr. George E. Wilson, Toronto, Benign Strictures of the Bile Ducts with a New Method of Treatment.

Dr. Clifford B. Walker, Los Angeles, A New Visual Phenomenon Useful as a Functional Test in Subjectively Studying Action of Eye Muscles and Retina.

Dr. Walter W. Chipman, Montreal, Canada, will deliver the annual oration on surgery, entitled "Our College Mandate—A Tribute to Allen B. Kanavel"; Dr. Isidore Cohn, New Orleans, will deliver the fracture oration on "The Evolution of Fracture Treatment." A new feature this year will be "midday round table conferences" Tuesday, Wednesday and Friday.

Congress of Anesthetists.—The seventeenth annual Congress of Anesthetists will be held in New York at the Hotel McAlpin, October 17-21. This congress is made up of the Associated Anesthetists of the United States and Canada, International Anesthesia Research Society, Eastern Society of Anesthetists and the Mid-Western Association of Anesthetists. The meeting will be dedicated to the memory of Sir Frederick W. Hewitt, London, anesthetist to Their Majesties George V. and Edward VII. Sir Frederick died in 1916. Laboratory demonstrations and special clinics will be presented several mornings at various hospitals. Speakers who will address the formal sessions include:

Dr. Edmund W. Lunney, St. John, N. B., Canada, Sir Frederick Hewitt, Anesthetist: His Life and Work.

Dr. Geoffrey Kaye, Melbourne, Australia, Scope and Utility of the New Anesthetic Techniques in Anesthesia.

Dr. J. B. W. ... Mexico, D. F., I. Accidents and Emergencies. II. Therapeutics Employed in Mexico.

Francis M. Whitacre, Ph.D., Cleveland, Experimental Investigations of Newer Anesthetics.

Drs. Ernesto Frias Meneses and S. Fernández, Santiago, Chile, Clinical and Experimental Observations on a Peculiar Type of Postoperative Pulmonary Atelectasis.

Dr. Perry P. Volpitta, Augusta, Ga., Treatment of Barbiturate Poisoning.

Dr. Russell F. Bonham, Houston, Texas, Helium as an Adjunct in Anesthesia, Especially from a Clinical Standpoint.

Drs. Ralph M. Tovell and Frederick C. Wilcox Jr., Hartford, Conn., Choice of Anesthetic Agents and Methods of Their Administration.

Foreign Letters

LONDON

(From Our Regular Correspondent)

Sept. 17, 1938.

Stored and Preserved Foods

The storage and preservation of foods, which is such a feature of modern civilization, has raised the question whether the treated foods are as nutritious as fresh foods. The Food Investigation Board has issued a report on the changes which all varieties of food undergo naturally and under the various methods of preservation. In addition to conducting investigations in England its experts visited laboratories abroad. The impression gained in the United States was that, while our country is in no way behind it in research on the handling and storage of foodstuffs, our application of science is not so forward. From time to time the members of the board have been asked whether food stored by modern methods, such as cold storage, gas storage and canning, is as nutritious as fresh foods. They referred the question to the Medical Research Council, which they thought more competent to deal with it, and on the authority of that body make the following statement:

"There is still so much to be learned about food and nutrition that it is impossible, in the present state of knowledge, to state categorically whether or not stored foods are as nutritious as fresh foods. Nor is it feasible to undertake research with a view to answering this question directly. Many years of intensive work on large groups of human beings would be entailed, and even then there would be little prospect of arriving at a definite decision, for further knowledge of the effect of dietary factors on nutritional processes would show that the results achieved would have to be reconsidered. Nevertheless, useful information can be obtained by comparing the chemical composition of stored foods with that of fresh foods, and the general conclusion can be accepted that relatively little less of known constituents is present in foods stored by modern methods. Moreover, in animals satisfactory nutrition has been maintained with diets composed solely of stored foods. The available evidence therefore suggests that modern methods of storing foods cause little depreciation in their nutritive value; in fact, it may be said that food of good initial quality that has been stored by the best modern methods is likely to be superior in many respects to similar food that, though still technically fresh, is in reality stale. One substance of important biologic significance, associated especially with fresh fruit and vegetables, namely vitamin C or ascorbic acid, is easily destroyed by heat, applied either in ordinary cooking or in canning; to a less extent vitamin B₁ is liable to be similarly affected."

THE STORAGE OF FISH

During the last ten years there has been an increase in the care with which fish is handled and stored on ice in trawlers. Storage in ice will keep fish fresh for from ten to twelve days. Beyond this period fish cannot be kept fresh, because bacteria can multiply at the temperature of melting ice, and some more powerful method is required. At the Tory Research Station the method has been worked out of freezing fish in brine at a temperature of -20°C . and storing them at the same temperature or, better, at a temperature of -30°C . White fish so treated retain their original freshness for at least six months. Indeed lemon soles have been kept at the station in a palatable condition for as long as two years. Thus a highly perishable article has been converted into one relatively imperishable. The industry is now considering the commercial possibilities of this method. The report recommends the freezing of that part of the trawler's catch which cannot be landed within twelve days. The fish should be absolutely fresh when frozen.

Test for Hydrogen Cyanide in Industry

The Department of Scientific and Industrial Research has issued a pamphlet describing a standard method for detecting hydrogen cyanide in industry. This gas is encountered in concentrations which may be dangerous in blast furnaces, dyestuff works, gas works and coke ovens, gilding works and gold mines. It is used in the fumigation of ships and buildings. In addition to the usual danger of inhalation there is danger to a person wearing an efficient respirator—absorption through the skin, which is greater if the skin is wet with sweat. The ordinary tests for hydrocyanic acid are not sufficiently sensitive to detect the low concentrations likely to be encountered in the atmosphere. Moreover, they are interfered with by the presence of other gases. The standard method of the department consists in drawing samples of the atmosphere to be tested through a piece of test paper impregnated with benzidine and copper acetate or with congo red and silver nitrate. The test papers are prepared from extra thick white filter paper; they are immersed in the solution, dried and then used immediately. The colors produced are compared with standards of varying depth which are supplied with the pamphlet. These, in conjunction with the number of strokes given to the pump, show the concentrations of hydrogen cyanide down to 1 in 100,000. One part in 50,000 will produce slight symptoms after several hours, and one part in 10,000 is dangerous after an hour.

Welfare in Factories

July 1 there came into operation a new factories act, which affects in a variety of ways the working conditions of nearly 6,000,000 persons. The object is to secure safe and healthy conditions of employment in some 250,000 factories (a term which now includes workshops). The immensity of the undertaking is shown by regulations covering such diverse fields as sanitary accommodation, conditions under which certain operations may be carried out at unfenced machinery, the provision of goggles or screens for protecting the eyes, the employment of young persons on night shifts, the calculation of overtime and the arrangement of intervals for meals and rest for women and young persons to meet seasonal or special pressure of work. Employers are required to post in their factories notices in a prescribed form specifying the scheme of working hours for women and young persons within the maximum limit and the intervals fixed for meals and rest. In general the permitted hours of employment for these workers will be reduced to forty-eight a week. Anything in excess will be overtime and will be strictly limited. Those under 16 will not be allowed to work overtime, and their working time has been reduced to forty-four hours a week. Women and young persons will not be allowed to begin work earlier than 7 a. m. or to end it later than 8 p. m., and they must all finish by 1 p. m. on Saturday. Those under 16 must end their work on other days by 6 p. m. Factory inspection has been intensified and the staff of inspectors increased.

Gastric Complaints of London Busmen

In a recent strike of London busmen the argument was used that their working conditions were so detrimental as to render them specially affected with gastric complaints. An investigation was therefore made by Dr. Bradford Hill (medical statistician) on behalf of the Industrial Research Board. He has made a report which shows that in 1933-1935 the omnibus drivers had a relative excess of gastric sickness (in proportion to all sicknesses) of from 12 to 14 per cent over the figure for tram-car drivers, while omnibus conductors had an excess of from 15 to 18 per cent over tram-car conductors. Expressed in another way, one day in six and one-half total days of sickness recorded by the two groups of omnibus workers was attributed to gastric causes, compared with one day in seven and one-half for tram-car workers. The report affirms that it is impossible to determine from the existing mortality statistics that the average life

of an omnibus worker is lower than that of other occupational groups. Indeed, figures show that drivers of motor vehicles and steam wagons have a better mortality than that of all occupied civilian males in England and Wales of the same ages. Since the omnibus strike a new agreement has been reached providing for improved terminal facilities and breaks in each spell of duty equivalent to not less than 5 per cent of the journey's time. An investigation is proceeding with a view to discovering the causes of the gastric sickness and measuring the influence, if any, on the omnibus workers of irregular meals, nervous strain, exhaust fumes and speedier service.

PARIS

(From Our Regular Correspondent)

Sept. 10, 1938.

Symposium on Cancer of the Breast

At the June 20 meeting of the French Association for the Study of Cancer a series of papers was read on the evaluation of transillumination as a diagnostic method and on the end results of operative treatment of cancer of the breast.

The first paper was by Dr. René Huguenin of the Paris Cancer Institute, who has used the transillumination method in 800 cases in six years. He said that it is necessary to change the older notions with regard to differentiating benign from malignant lesions in the female breast by inspection and palpation. In a large number of cases of early involvement in which the diagnosis of a malignant process was confirmed by biopsy, palpation showed that the tumor was nodular and sharply circumscribed by a perineoplastic reaction of the surrounding stroma. This physical characteristic has hitherto always been considered typical of a benign condition. In former times it was taught that a malignant lesion in its early stages was not adherent to the overlying skin, so that dimpling did not follow when the skin was grasped between the thumb and index finger. This negative result of palpation meant that the tumor was located deeply in the gland and separated from the skin by the premammary fat. It is evident at present that even the most painstaking examination will not be able to determine definitely whether a deeply seated neoplasm is a simple cyst or a neoplastic nodule, because of the manner in which the overlying fat masks such a lesion. It was also formerly taught that a diffuse but extensive induration occupying a quadrant or more of the breast was malignant. Many such growths have been needlessly operated on. At the Paris Cancer Institute a number of cases have been observed of such massive indurations due to benign canalicular and acinous hyperplasia. It would seem paradoxical, but recent observations show that extensive and noncircumscribed indurations are frequently benign, whereas small, sharply demarcated nodules are frequently malignant. Even with regard to enlargement of the axillary lymph nodes, our former notions must be revised. Recurrent attacks of hyperplastic mastitis can be accompanied by indurated, painless, axillary lymph nodes, while in some cases of early cancer no involvement of lymph nodes is apparent even on histologic examination. In many cases of cancer the enlarged lymph nodes show no evidence of malignancy. It may even happen that they are tuberculous, as was found by Huguenin and Redon in several cases. The clinician should be warned against giving androgenic or estrogenic substances when a diagnosis of a single or multiple cyst has been made, because there is a possibility of the coexistence of a cancer in the wall of such a cyst or even in simple massive hyperplasia.

After trying all other recently advocated methods, such as plain roentgen examination and injection of opaque media, Huguenin now employs only transillumination, the technic of which can easily be learned by the surgeon. The results of this newer method of diagnosis are not infallible. At the Paris Cancer Institute they were verified by histologic exami-

nation in only 80 per cent of the cases. Perhaps the percentage of erroneous diagnoses can be reduced as experience increases and the technic of the source of illumination is perfected. Some of the processes which were regarded as malignant after transillumination proved to be tuberculous mastitis or hemorrhagic cyst, potentially malignant conditions, so that operative intervention was not in vain. The chief value of transillumination is that it serves as a guide for treatment. If there is no evidence of opacity, the patient should not be operated on but should be followed and reexamined from time to time. If, however, transillumination reveals a more or less extensive opacity, so that a diagnosis of cancer appears probable, a biopsy should be done if possible before operation. If a diagnosis of cancer has been made by palpation and transillumination gives a negative result, biopsy should nevertheless be done as soon as possible. Transillumination is of value in indicating the seat of a lesion, so that radical operations can at times be avoided. Often transillumination is negative and the clinical examination positive. In such cases, only biopsy can decide which diagnosis is correct. The objection may be raised against transillumination that, after all, a preoperative biopsy must be done if the results of the clinical and the transillumination examination differ. The chief advantage of transillumination is that it serves as a guide to the location of a lesion which should be subjected to biopsy, thus avoiding the removal of a cyst or hyperplastic nodule and leaving a small cancer which is visible by transillumination.

MICROSCOPIC EXAMINATION DURING OPERATION

A second paper, on better end results as the result of microscopic examination during operation, was read by Dr. Georges Lardennois of Paris. The prognosis of cancer of the breast before involvement of the axillary lymph nodes has taken place is as favorable as that of the majority of other cancers. Since 1923 Dr. Lardennois has insisted on a microscopic examination being made during all operations on the breast. Up to 1934 Professor Leroux examined 118 cancers by means of the freezing technic; only once was an erroneous diagnosis made, and this was corrected as soon as more material for study was available. Since 1934 a special technic termed *ultropaque* has been used by Professor Leroux, and every one of his decisions as to whether specimens examined during operation indicated a benign or malignant condition has been confirmed by later (postoperative) microscopic examination. Up to Feb. 1, 1934, a benign condition was found in fifty-four and a malignant process in sixty-four cases. Since 1934, as a result of earlier exploration and immediate microscopic examination during operation, the percentage of lesions found to be benign has increased. In seventeen of the 118 cases in which operation was performed before 1934, i. e. four and one-half years before the follow-up statistics were collected, the diagnosis was doubtful at the time of operation and it has been impossible to determine the end results. In six others an erroneous diagnosis had been made. The general practitioner's attention ought to be called to the necessity of not waiting to make a diagnosis until retraction of the nipple, wrinkling of the skin overlying the suspected neoplasm and palpable axillary lymph nodes are found. When these exist, it is too late to expect a favorable end result, because internal metastases have already taken place. With the most malignant conditions all these signs may be lacking. When serous or hemorrhagic exudation from the nipple is seen, no one is able to say whether the intracanalicular neoplasm is benign or malignant. In four of seven such cases the process was found to be benign, and in three it was malignant. The clinical diagnosis of a tumor of the breast is presumptive and becomes positive only after microscopic examination.

Dr. Lardennois criticized the method so often employed of making a biopsy several days before operation, because the traumatism, formation of hematoma and local congestion appear

to favor visceral metastasis. Before he adopted the method of always examining the specimens removed at the beginning of an exploratory operation, he observed some very unfavorable end results when an interval of several days was allowed to elapse between the biopsy and the operation itself. Of sixty-four patients (eight of whose neoplasm was intracanalicular) operated on prior to 1934, twenty-six, including three males, were living from four and one-half to fifteen years after operation. Such favorable end results would be even better if every general practitioner insisted on immediate exploration and removal of every suspected tumor of the breast. The incision for exploration employed by Dr. Lardenois is a submammary one, and the suspected area is removed with the electric bistoury. While the vessels are being ligated, the microscopic examination can be made and the decision reached as to whether a radical operation should be done.

END RESULTS

The third paper was read by Professor Ducuing of Toulouse and cited the end results in 243 cases of cancer of the breast in which operation had been done in his clinic. The diagnosis of a malignant process was confirmed by microscopic examination in every case. In every such survey of end results it is essential to exclude cases in which only palliative operations were done as compared to those in which the operation was radical. There were forty-six cases in which simple palliative procedures were employed to remove extensive areas of ulceration and control bleeding and no attempt was made to extend the operation to the axillary lymph nodes. Of the forty-six apparently hopelessly ill patients, 30 per cent lived more than three years and 13 per cent more than five years. When a radical operation was performed, it was found that 40 per cent of the patients presented no evidence of recurrence within three years and 31 per cent from five to nine years after operation. This more than five year survival percentage is perhaps lower than that of some other clinics but appears satisfactory when one takes into consideration the fact that the wider indications for radical operation made it possible to include many patients who might have been refused such a procedure by other surgeons. This survival rate is also perhaps lower than that for irradiation alone, but not all the patients treated by this method had a microscopic examination as a control. In the future, perhaps a higher rate of five year survivals may be attained by combining radical procedures with postoperative irradiation.

The end results of the operative treatment of cancer of the breast at the Curie Foundation and at the Hôtel-Dieu were presented by Dr. André Tailhefer of Paris. During the past eleven years, 160 cancers of the breast have been operated on. The end results in forty-six patients who have not shown any signs of recurrence from five to eleven years after operation were the only ones submitted. An incision which permitted removal of a large cutaneous area was used in all cases. In eleven of the forty-six cases microscopic examination of the axillary lymph nodes failed to reveal any evidence of cancerous involvement. Ten of the eleven patients are apparently well from five to nine years after operation. Only one patient died of sternal metastases; his death occurred a year after operation. Of thirty-two patients whose axillary lymph nodes were already involved by extension from the breast cancer, fourteen are apparently cured. The interval since operation varies from eleven years and two months to eleven years and four months. A study as to the incidence of metastases in the remaining eighteen cases shows that the supraclavicular and intrathoracic lesions are the most common and that the incidence is relatively high when the cancer is located in the inner half or in the deeper portions of the breast. Forty-two of the 160 patients operated on during the past eleven years showed absence of any involvement of the axillary lymph nodes. There are two forms of supraclavicular metastases; in one the lymph nodes are deeply located and inaccessible, whereas for the other,

situated well above the clavicle, removal is still possible. During recent years, microscopic examination of tissue removed during the operation, as recommended by Lardenois, has been employed in the majority of cases. The conclusions reached by Dr. Tailhefer were that radical operation will be followed by cure in a relatively high percentage of cases provided that only favorable cases are selected for operation; hence he carried out the radical procedure only in cases in which the tumor did not exceed from 4 to 5 cm. in diameter and there was slight or no involvement of the axillary lymph nodes. If microscopic examination confirms the absence of such an extension, nothing further is done. If, however, the axillary nodes are shown to be invaded, postoperative roentgen or radium treatment is directed toward the supraclavicular and internal mammary chains of lymph nodes. To patients presenting a tumor more than 4 or 5 cm. in diameter or accompanied by evident involvement of the axillary nodes, seen on gross or microscopic examination, preoperative roentgen irradiation is given for a month before the radical operation.

DIFFICULTIES OF DIAGNOSIS

The next paper was by Prof. Henri Hartmann and called attention to the difficulty of making a diagnosis in cases of mammary tuberculosis of the pseudoneoplastic type, in certain cases of localized nontuberculous chronic mastitis and in cases of chronic abscess of the breast. He was opposed to preoperative biopsy or removal during operation of tissue for microscopic examination, even with the more rapid methods now employed, because of the danger of the migration of cancer cells into lymph spaces which had been opened during the preliminary exploratory procedure. Another objection is that if the pathologist gives a negative opinion of the specimen examined at operation, the tissue submitted to him may not include the cancer area. Professor Hartmann prefers to remove a large segment of the breast at the first operation, i. e. to do a partial resection then and a more radical one later. Some patients may object to two operations, but his end results in thirteen cases, with two eight year survivals and one ten year survival, show that the two step procedure has many advantages. Recurrence has been observed as late as ten years or more after a radical operation. Although local recurrence may not be evident, many patients die of visceral metastases. Irradiation alone is to be recommended in cases of diffuse carcinomatous mastitis and in cancers with extensive ulcerations.

INVOLVEMENT OF AXILLARY NODES

The last paper in the symposium was read by Dr. Desmarest, who agreed with previous speakers as to the part played by involvement of the axillary lymph nodes in the prognosis of cancer of the breast. Of 100 patients on whom the radical operation had been performed by him, fifty-four died within the first three years, fourteen during the next two years, one during the sixth year and three during the seventh year. It is misleading to state that a patient has survived a certain number of years after operation. It would be more correct to state when the first signs of a recurrence had appeared, because in a number of cases life becomes insupportable two or three years before death. Dr. Desmarest's results were so poor because the axillary nodes were involved at an early period in the evolution of the cancer in a large percentage of his cases. He expressed the opinion that when there is evidence of advanced involvement of these nodes, a radical operation is not only of no avail but may do more harm than good. The results of palliative treatment of inoperable cancers, as Professor Ducuing had shown earlier in the symposium, were almost as good as those after attempts to do a radical operation. Dr. Desmarest said that if there is no involvement of the axillary nodes, removal of the breast alone is indicated. If the nodes are already involved, there is a risk of dissemination of the cancer to the supraclavicular lymph nodes or even to the viscera during a radical operation.

JAPAN

(From Our Regular Correspondent)

Aug. 29, 1938.

The Decrease in Medical Students

The number of candidates for medical schools this year suddenly decreased. There were only 1,241 candidates for thirteen medical colleges. Of these colleges, eight had far fewer candidates than they had expected. This may have been due in part to the fact that all the colleges give their examinations on the same day, but the deepest cause must be the unpopularity of medical practice at present. Medicine in this country has long been the most favored profession, at which practitioners succeeded in accumulating wealth. Many bright students applied to the medical colleges. Great physicians did much to raise the level of medicine in this country to that in other countries in a short period. People in general began recently to have a different idea of medicine. They now insist that it ought not to be a free profession and that medical practice should be strictly controlled by the government. This tendency is a menace to physicians. With the development of national health insurance, the income of physicians decreased, and people gradually began to prefer a hospital physician to an independent practitioner. There are, the health office reports, 57,581 physicians, of whom 51,597 are practitioners. Less than half of the practitioners are independent, and the rest are employed in hospitals on a salary basis. As future physicians will be merely salaried men, graduates of high schools prefer other more promising professions. A conference of the presidents of all government universities was held to talk over this matter, and they agreed to propose to the education office measures to meet the situation.

The Board for Disabled Soldiers

The board for disabled soldiers was recently created as a branch of the welfare office, and 35,300,000 yen was appropriated by the Diet for this fiscal year. General Honjo was appointed president. The chief aim of this institute is to give disabled soldiers and their families ample relief, medical and otherwise. This year there are to be established twenty-five new sanitariums, each able to accommodate 500 persons with tuberculosis, at a cost of 24,610,000 yen. * A home for soldiers suffering from mental disease will be established as the next work. Ten sanatoriums will be established at hot springs near the division headquarters, where disabled soldiers will be cared for and treated, each for about two months. This year about 3,000 men will be admitted. Until the completion of all the establishments, the private institutes throughout the country will be entrusted with the treatment of soldiers. A home for crippled soldiers in Tokyo is to be established by a few business men at their own expense, independently of the government institute. Two million yen will be contributed for the fund, and the building is expected to be completed by the end of this year.

Venereal Disease Among Returned Soldiers

The present Sino-Japanese trouble is thought to have caused an outbreak of venereal diseases when so many soldiers returned from the front after a long absence from home. A sum of 1,343,654 yen was given by the government to be used in preventing these diseases. As the first measure, ninety-four venereal disease clinics are to be built in the larger cities. Returned soldiers will be examined at these clinics before discharge, and those infected will not be discharged until they have completely recovered.

Physical Condition of Shop Workers

The results of the physical examination of conscripts this year revealed as usual many defects in their physical condition. The conscripts fall into two groups: (1) those who left primary school at the age of 12 and (2) those who left at the age of 14. The conscription examinations show that there is little difference between the two groups in the rural areas,

where the conscripts do not become shop workers, but a great deal in the cities and manufacturing centers. In cities, workers less than 12 years of age work under very unhealthy conditions, while in the farming villages they work under favorable conditions. The following statistics pertain to the conscription examinations of the young shop workers in the larger cities. Of 997 boys who had left the eight year primary school and were engaging in business, 317 were passable and 323 were second grade passable (64 per cent), while 357 were not able to pass (35.7 per cent). Of the same number of those who left the six year school, 286 were passable and 282 were second grade passable (56.7 per cent), while 429 did not pass. Physical development in this country is complete for the female at the age of 19 and for the male at the age of 20. The present habit of employing young boys and girls in shops or offices is far from ideal, for they are often obliged to work from morning till night without any time for rest. Some of them are forced to go in the evening to the young men's schools, which close at 9 o'clock. It is reported that the welfare department has drafted a law for protecting young shop workers.

Research Institution on Mount Fuji

The building of the Japanese institute for research in military aviation medicine, under construction since last summer on the top of Mount Fuji (3,778 meters), was completed in July. The opening ceremony was held in August, with many prominent military surgeons present. The costly building contains fourteen rooms with complete protection against cold, and it is situated next door to the station belonging to the Central Meteorologic Observatory. There will be a standing staff consisting of two army surgeons, and two men from the military medical school will alternate yearly as assistants. The chief research will be on such subjects as the physiologic state of the human body at a high altitude and the hygiene of aerial navigation. This is the first institution of this kind in the country.

Waichiro Okada Is Dead

Dr. Waichiro Okada, honorary professor of the Tokyo Imperial University and president of the Showa Medical College, died of asthma June 30 at the age of 75. He was born in a little town on Shikoku Island, in middle Japan. He graduated with honors from the medical college of the Tokyo Imperial University in 1889; in 1895 he was appointed assistant professor in the department of surgery, and the next year he was sent to Germany to study otorhinolaryngology, staying there about five years. On his return to the Tokyo Imperial University from abroad in 1900, he opened the first independent department of otorhinolaryngology at a university in this country. The next year he was appointed professor. He retired from the university in 1924. During his twenty-five years there he did much for the development of otorhinolaryngology. After retiring he founded the Showa Medical College in Tokyo. He was for forty years the president of the Japan Society of Otorhinolaryngology. He was also a politician. He offered his services to the municipal administration of the city of Tokyo and was an assemblyman for many years.

Marriages

RICHARD HARDY APPLE, Culver, Ind., to Miss Ella Frances Parker of Salisbury, N. C., in Albemarle, N. C., September 3.
PROSSER HARRISON PIOT, Richmond, Va., to Miss Elmyra Davidson Williams of Wytheville, September 3.
GERHARD K. MANSKE, Texas City, Texas, to Miss Hallie Andrews of Wichita Falls, in Austin, June 25.
GILLIAM SWINK HICKS, New York, to Miss Cornelia Griffin Williams of Memphis, Tenn., July 2.
JACOB H. KRESS, Thomasville, N. C., to Dr. Esta Joyce Levy of Suffolk, Va., August 11.

Deaths

Charles Phillips Emerson • Indianapolis; Johns Hopkins University School of Medicine, Baltimore, 1899; professor of medicine and dean, Indiana University School of Medicine, 1911-1932, and research professor since 1932; formerly associate in medicine at his alma mater; assistant professor of medicine at Cornell University, 1909-1910; member of the Association of American Physicians; past president of the Association of American Medical Colleges and the National Committee for Mental Hygiene; superintendent of the Clifton Springs (N. Y.) Sanitarium, 1908-1911; during 1931 and 1932 was a member of a commission, sponsored by the Laymen's Foreign Mission Inquiry, to study educational and medical missions in the Orient; in 1934 was awarded the honorary degree of doctor of science by Amherst College, Amherst, Mass., his alma mater; author of "Pneumothorax," "Clinical Diagnosis," "Hospitals for Children" and "Essentials of Medicine" and joint author of "Emerson and Betts Physiology and Hygiene," "Physical Diagnosis," "The Nervous Patient" and "Text Book of Medicine"; aged 66; died, September 26, of bronchopneumonia.

Thomas Richmond Boggs • Baltimore; Johns Hopkins University School of Medicine, Baltimore, 1901; at various times associate professor of medicine, associate professor of clinical medicine, instructor and associate in medicine at his alma mater; member and past president of the Association of American Physicians; member of the American Society for Clinical Investigation; was decorated for services during the World War and later was a colonel in the medical reserve corps; on the staffs of the Johns Hopkins Hospital, Baltimore City Hospital, Church Home and Infirmary, Union Memorial Hospital and the Hospital for Women; consultant to the Veterans Bureau at Washington; aged 62; died, September 2, at Fredericksburg, Va.

Leroy Watkins Hubbard • Mount Vernon, N. Y.; University of the City of New York Medical Department, 1883; director of the extension work for the Warm Springs Foundation in Georgia, where he was formerly surgeon in chief; connected with the city health department from 1897 to 1914; member of the American Academy of Orthopedic Surgeons; in 1934 was awarded the golden key of merit by the American Congress of Physical Therapy; aged 81; died, August 31, in a sanitarium at Clifton Springs, N. Y., of arteriosclerotic heart disease and coronary occlusion.

Thomas Archibald Davis • St. Petersburg, Fla.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1885; member of the Illinois State Medical Society; fellow of the American College of Surgeons; formerly professor of surgery and clinical surgery at his alma mater; at one time president and professor of surgery at the Illinois Post-Graduate Medical School; for many years surgeon to the Cook County Hospital and the West Side Hospital, Chicago; aged 80; died, September 19, at his summer home in Delavan, Wis.

Henry Howard Whitehouse • New York; College of Physicians and Surgeons, Medical Department of Columbia College, New York, 1889; at one time professor of dermatology at the New York Post-Graduate Medical School, Columbia University; instructor of dermatology and syphilology at Cornell University Medical College, 1902-1907; member of the American Dermatological Association; served in various capacities on the staff of the New York Skin and Cancer Hospital; aged 74; died, August 24, in Mystic, Conn.

Frederick Henry Flaherty • Syracuse, N. Y.; Syracuse University College of Medicine, 1896; member of the House of Delegates of the American Medical Association, 1927-1932, 1935-1937; past president of the Medical Society of the State of New York and of the Onondaga County Medical Society; professor emeritus of clinical surgery at his alma mater; fellow of the American College of Surgeons; aged 64; surgeon to the Syracuse Memorial Hospital and St. Joseph's Hospital, where he died, September 7, of cerebral hemorrhage.

Raphael Burke Durfee • Bisbee, Ariz.; Georgetown University School of Medicine, Washington, D. C., 1900; past president of the Arizona Public Health Association; at one time professor of anatomy at the College of Physicians and Surgeons, Los Angeles; city bacteriologist for Los Angeles, 1908-1916; city and county health officer; Veteran of the Spanish-American and World wars; aged 62; died, July 24, of coronary thrombosis.

Maurice Farvish Lautman • Hot Springs National Park, Ark.; Yale University School of Medicine, New Haven, Conn., 1911; consultant to the U. S. Public Health Service Clinic;

served during the World War; on the staff of the Levi Memorial Hospital; author of "Arthritis and Rheumatic Disease"; aged 48; died, September 24, of coronary thrombosis.

Charles William Stevenson • Wichita Falls, Texas; University of Texas School of Medicine, Galveston, 1912; fellow of the American College of Physicians; served during the World War; medical director and owner of Dr. White's Sanitarium and on the staff of the Wichita General Hospital; aged 49; died, July 31, of pneumonia.

William Matthew Dugan • Battle Creek, Mich.; University of Michigan Medical School, Ann Arbor, 1916; fellow of the American College of Surgeons; past president of the Calhoun County Medical Society; on the staff of the Leila Y. Post Montgomery Hospital; aged 53; died, August 22, of abdominal carcinoma.

William J. Trefethen, Wilton, Maine; College of Physicians and Surgeons, Baltimore, 1894; member of the Maine Medical Association; formerly member of the state legislature and senator; aged 71; on the staff of the Franklin County Memorial Hospital, Farmington, where he died, July 24, of cerebral hemorrhage.

Bertell Laroy Talbot, Milford, N. H.; Harvard University Medical School, Boston, 1896; member of the Massachusetts Medical Society; at one time member of the board of health of Peterboro; served during the World War; formerly a member of the Veterans Bureau; aged 66; died, July 14, of heart disease.

John Aloysius Farrell • West Chester, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1898; past president of the Chester County Medical Society; served during the World War; on the staff of the Chester County Hospital; aged 63; died, July 30, of coronary thrombosis.

Claude Dickson Scaff, Clarksville, Texas; Kentucky School of Medicine, Louisville, 1905; member of the State Medical Association of Texas; past president and secretary of the Red River County Medical Society; county health officer; aged 59; died, July 26, of rheumatic heart disease.

Reeves Bailey Van Duzer • East Orange, N. J.; Columbia University College of Physicians and Surgeons, New York, 1930; on the staff of the Montclair (N. J.) Community Hospital; aged 34; died, July 7, in the Orange (N. J.) Memorial Hospital of acute nephritis and uremia.

John Blois Watson • Raleigh, N. C.; University of North Carolina School of Medicine, Raleigh, 1908; formerly professor of materia medica, pharmacology and therapeutics at the Leonard Medical School; aged 53; died, July 15, in the Rex Hospital of septic endocarditis.

Francis Michael C. Rochford, Brooklyn; Long Island College Hospital, Brooklyn, 1903; member of the Medical Society of the State of New York; served during the World War; director of the department of pediatrics, Misericordia Hospital; aged 60; died, July 31.

Samuel Alaga Roe, Corvallis, Ore.; Missouri Medical College, St. Louis, 1897; New York Homeopathic Medical College and Hospital, 1898; member of the Pacific Coast Oto-Ophthalmological Society; formerly on the staff of the Corvallis General Hospital; aged 61; died, July 14.

John Davis Colson, Pageland, S. C.; Medical College of the State of South Carolina, Charleston, 1909; served during the World War; at various times member of the town council and county board of education; aged 49; died, July 18, in the McLeod Infirmary, Florence, of nephritis.

Robinette Burns Hayes, Hillsboro, N. C.; University of Maryland School of Medicine, Baltimore, 1906; member of the Medical Society of the State of North Carolina; served during the World War; aged 61; died, July 16, in the Watts Hospital, Durham, of cholelithiasis.

William Alex Gordon, Hagerstown, Md.; College of Physicians and Surgeons, Baltimore, 1893; member of the Medical and Chirurgical Faculty of Maryland; past president and secretary of the Washington County Medical Society; aged 71; died in July of endocarditis.

Harold James Durant • Paterson, N. J.; Tufts College Medical School, Boston, 1927; fellow of the American College of Surgeons; served during the World War; aged 41; on the staff of St. Joseph's Hospital, where he died, July 15, of typhoid and pulmonary embolism.

Luke Robinson, Covington, Ga.; Southern Medical College, Atlanta, 1893; member of the state board of medical examiners; member of the city council and board of education; aged 69; died, July 23, in the Emory (Ga.) University Hospital of cirrhosis of the liver.

Arthur Thurston Newcomb * Pasadena, Calif.; Baltimore Medical College, 1893; served during the World War; member of the American College of Physicians; on the staff of the Huntington Memorial Hospital; aged 65; died, July 18, of cerebral embolism.

Roy Raymond Bair, Newark, N. J.; Chicago College of Medicine and Surgery, 1916; New York Homeopathic Medical College and Flower Hospital, New York, 1918; aged 57; died, July 23, in the Presbyterian Hospital of septicemia following a prostatectomy.

Joseph C. E. Fritch, Cleveland; Cleveland College of Physicians and Surgeons, Medical Department Ohio Wesleyan University, 1896; aged 71; on the staff of the Lutheran Hospital, where he died, July 25, of myocarditis and gangrenous appendicitis.

Henry Gatrell, Fairfield, Fla.; Medical Department of Tulane University of Louisiana, New Orleans, 1898; member of the Florida Medical Association; aged 64; died, July 24, in a hospital at Orlando of cirrhosis of the liver and arteriosclerosis.

Paul Renger * Hallettsville, Texas; Medical Department of Tulane University of Louisiana, New Orleans, 1901; owner of the Renger Hospital; aged 61; died, July 26, in the Nix Hospital, San Antonio, of nephritis, myocarditis and bronchiectasis.

Mark William Baxter, Salt Lake City; Drake University Medical Department, Des Moines, Iowa, 1892; member of the Utah State Medical Association; medical director of the Mountain View Sanatorium; aged 88; died, July 22, of arteriosclerosis.

Bernard Leo O'Donnell, New York; New York University Medical College, 1898; member of the Medical Society of the State of New York; aged 65; died, July 18, in St. Francis Hospital, of perirectal abscess and cardiorenal arteriosclerosis.

Richard Ellwood Peteferd, Springfield, Ohio; Ohio Medical University, Columbus, 1906; member of the Ohio State Medical Association; aged 55; died, July 29, in the City Hospital of carbuncle with multiple abscesses of kidneys and lungs.

Fred Allison Bower, Uhrichsville, Ohio; Ohio State University College of Medicine, Columbus, 1925; member of the Ohio State Medical Association; aged 38; died, July 25, in the Twin City Hospital, Dennison, of malignant hypertension.

Walter Hugo Rosenfield, Louisville, Ky.; University of Louisville Medical Department, 1907; member of the Kentucky State Medical Association; served during the World War; aged 59; died, July 5, in St. Mary and Elizabeth Hospital.

John Silverwood Sutcliffe, El Dorado, Kan.; Missouri Medical College, St. Louis, 1898; Marion-Sims College of Medicine, St. Louis, 1899; aged 77; died, July 19, in the Susan B. Allen Memorial Hospital of cerebral hemorrhage.

Henry Harris * San Francisco; Johns Hopkins University School of Medicine, Baltimore, 1899; formerly associate clinical professor of medicine, University of California Medical School; aged 63; died, July 7, of coronary disease.

Edward Carroll Brannon, Waco, Texas; Baylor University College of Medicine, Dallas, 1913; member of the State Medical Association of Texas; aged 48; died, July 23, in a hospital at Fort Lyon, Colo., of perforated gastric ulcer.

Reuben Hill Born, Montoursville, Pa.; Bellevue Hospital Medical College, New York, 1887; member of the Medical Society of the State of Pennsylvania; aged 73; died, July 14, of arthritis, arteriosclerosis and myocarditis.

William Balass Yoakley, Wilmington, Ohio; Howard University College of Medicine, Washington, D. C., 1915; member of the Ohio State Medical Association; aged 63; died, July 9, of cerebral hemorrhage.

John Gerald Bowers, Muskegon, Mich.; University of Minnesota Medical School, Minneapolis, 1934; member of the Michigan State Medical Society; aged 31; was killed, July 8, in an automobile accident.

Henry Anthony Merkel * Wilmington, Ill.; University of Maryland School of Medicine, Baltimore, 1916; served during the World War; for many years health officer; aged 47; died, July 26, of heart disease.

Arthur Sanders Bean, Morrisville, Vt.; New York Medical College and Flower Hospital, New York, 1916; member of the Vermont State Medical Society; aged 63; died, July 23, of cerebral hemorrhage.

Frank Maurice Boonstra, Muskegon, Mich.; Rush Medical College, Chicago, 1929; member of the Michigan State Medical Society; aged 36; died in July of injuries received in an automobile accident.

Frank Winthrop Smith, Red Oak, Iowa; State University of Iowa College of Medicine, Iowa City, 1894; member of the Iowa State Medical Society; aged 68; died, July 6, of heart disease.

Joseph A. Sesta * Jersey City, N. J.; George Washington University School of Medicine, Washington, D. C., 1922; aged 43; died, July 21, in the Christ Hospital of cerebrospinal meningitis.

Edward Fyndoll Wright, Greenville, Texas; Memphis (Tenn.) Hospital Medical College, 1900; past president of the Hunt County Medical Society; aged 64; died, July 9, of heart disease.

James O'Dell Rhea, Linden, Ind.; Medical College of Indiana, Indianapolis, 1902; veteran of the Spanish-American and World wars; aged 63; died, July 30, of cerebral hemorrhage.

Waite Leonidas Lambert, Asheboro, N. C.; Jefferson Medical College of Philadelphia, 1921; formerly county coroner; aged 44; died, July 17, in Asheville of pulmonary tuberculosis.

Charles A. De Witt, Los Angeles; Bennett College of Eclectic Medicine and Surgery, Chicago, 1897; aged 69; died, July 7, in the General Hospital of a self-inflicted bullet wound.

John Tillman Mills, Sasakwa, Okla.; Memphis (Tenn.) Hospital Medical College, 1905; aged 72; died, June 13, in the Veterans Administration Facility, Muskogee, of senility.

Richard Vance Spencer, Chicago Heights, Ill.; University Medical College of Kansas City, Mo., 1907; served during the World War; aged 59; died, July 11, of pneumonia.

Millard Louys Beuler, Cincinnati; University of Cincinnati College of Medicine, 1925; aged 39; died, July 3, of amyloidosis of the liver and spleen, with osteomyelitis.

George D. Lezotte, Muscatine, Iowa; Rush Medical College, Chicago, 1881; member of the Iowa State Medical Society; aged 81; died, July 4, of cardiovascular renal disease.

Frederick W. McKnight, Mesa, Ariz.; George Washington University School of Medicine, Washington, D. C., 1909; aged 63; died in July of hypertensive cardiorenal disease.

Ernestine Julia Hicks Garl, St. Maries, Idaho; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1889; aged 79; died, July 6, of endocarditis.

Jacob Wickerham Davis, Hawthorne, Nev.; Physio-Medical College of Indiana, Indianapolis, 1889; aged 85; died, July 2, of hypertrophy of the prostate and uremia.

Daniel Fitz Randolph, Waldron, Ind.; Medical College of Indiana, Indianapolis, 1888; aged 84; died, July 13, of chronic myocarditis and acute dilatation of the heart.

Lewis Wilson Berry, Trego, Wis.; Indiana College of Medicine and Midwifery, Indianapolis, 1881; aged 89; died, July 19, of myocarditis and arteriosclerosis.

Herman Leo Nahin, Milwaukee; College of Physicians and Surgeons of Chicago, 1895; aged 73; died, July 4, of coronary thrombosis, arteriosclerosis and hypertension.

Antoinette J. Hutchings, Lodi, Calif.; California Medical College, San Francisco, 1896; aged 84; died, June 25, in a hospital at Stockton of arteriosclerosis.

Charles Edmond Verge, Quebec, Que., Canada; M.B. Laval University Faculty of Medicine, Quebec, 1904, and M.D. in 1906; aged 56; died, July 10.

Otho H. Witcher, Sweet Springs, Mo.; American Medical College, St. Louis, 1889; aged 68; died, July 11, of chronic nephritis, cystitis and prostatitis.

Owen County Rees, Stratford, Ont., Canada; Chicago Homeopathic Medical College, 1887; served during the World War; aged 73; died, July 28.

William Stowe Fowler, San Marino, Calif.; College of Physicians and Surgeons of Chicago, 1888; aged 81; died, June 5, of aortic stenosis.

James Henry Greenwood * Detroit; Detroit College of Medicine, 1894; aged 74; died in July of carcinoma of the prostate.

Granville Ralph Todd, Knoxville, Tenn.; Tennessee Medical College, Knoxville, 1908; aged 60; died, July 6, of heart disease.

Norman R. Henderson, London, Ont., Canada; Queen's University Faculty of Medicine, Kingston, 1895; died, July 15.

David Ford * De Soto, Mo.; Barnes Medical College, St. Louis, 1900; aged 64; died, July 16, of chronic myocarditis.

Francis Wesley Forge, Toronto, Ont., Canada; University of Toronto Faculty of Medicine, 1919; aged 43; died, July 11.

J. F. Hartman, Glenville, W. Va. (licensed in West Virginia under the Act of 1881); aged 81; died, July 11.

John W. Graham, Early, Iowa (licensed in Iowa in 1886); aged 79; died, July 10, of cerebral hemorrhage.

Correspondence

ANIMAL EXPERIMENTATION IN CALIFORNIA

To the Editor:—Our attention has been called to a paragraph in an editorial which appeared in *THE JOURNAL*, February 19, which reads:

In 1932 and subsequently, a determined attempt was made to interfere with the use of dogs from the San Francisco pound, by the medical schools in the San Francisco Bay area. This attempt was frustrated by the combined vigilance of the medical profession and public health authorities.

From this quotation it must be inferred that the San Francisco pound was until 1932 providing dogs for use of medical schools; that an attempt was made to stop this practice, and that the attempt failed. Nothing could be further from the truth. As a matter of fact the opposite is true. Neither dogs nor any other animals have ever been provided by the San Francisco pound for medical schools. In 1932 an attempt was made to obtain dogs from the San Francisco pound for such purposes but it raised such a storm of protest that the matter was dropped. Incidentally it resulted in the addition of the following section to the pound ordinance:

SECTION 27. If the poundkeeper, or any one in his employ, shall knowingly sell or give any impounded animal to any person, firm, corporation, association, medical college or university of the state for the purpose of animal experimentation, the offender shall be guilty of a misdemeanor.

Any person, firm or corporation who, by or through fraud, misrepresentation, coercion or threat, induces any violation of the foregoing provisions, shall also be guilty of a misdemeanor.

This ordinance is in effect and has been since Sept. 27, 1932.

THE SAN FRANCISCO SOCIETY FOR THE
PREVENTION OF CRUELTY TO ANIMALS.
POUNDKEEPER.

CHARLES W. FRIEDRICH, S.,
Secretary and Manager.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

RAGWEED DESTRUCTION—DISTRIBUTION OF POLLEN

To the Editor:—1. Have any states or communities enacted laws requiring the destruction of ragweed? 2. If so, how successful have they been? 3. Have campaigns for the eradication of ragweed by the payment of a certain bounty per hundred pounds collected proved effective? 4. Has the expense of such campaigns been great? 5. In how close proximity to a field of pollinating ragweed must a person allergic to it be in order to be affected?

M.D., Massachusetts.

ANSWER.—1 and 2. As far as has been determined, no state or community has enacted a weed law specifically naming ragweed and requiring its destruction. Many states have laws covering a limited list of so-called noxious weeds the destruction of which is mandatory. Ragweed is listed as a noxious weed in some state weed bulletins but in such instances the term "noxious weed" is not construed as in the sense of mandatory destruction. At the 1937 session of the Illinois state legislature a definite effort was made by certain interested persons to have ragweed included in the list designated as noxious weeds. The legislature thought best not to include it because of the large acreage of ragweed and the consequent heavy burden that would be imposed on land owners. However, a resolution was passed requesting the governor to designate certain days in August as "Weed Destruction Days" and authorizing the director of the state department of agriculture "to consider the establishment of a comprehensive weed control program specifically to encourage the destruction of ragweed, horseweed, poison ivy, etc." Almost all states and municipalities have laws covering the control of weeds on highways.

The provisions of these laws are usually carried out, resulting in the mowing of all tall weeds, including ragweed, from once to several times a year on streets, alleys and highways. Many municipalities also have laws requiring owners of property, including vacant property, to keep all weeds under control. The laws empower the city officials to cut the weeds if the owner fails to do so and to charge the expense to the owner. Such laws, if properly enforced, would result in effective control of ragweeds within the limits of most cities. But these laws are rarely enforced.

3 and 4. As far as can be ascertained, only one community has dealt with the ragweed problem on the basis of payment of bounty. This city offered a small bounty for each bundle of fifty ragweeds. Less than \$1,000 had been appropriated for the purpose and the money was exhausted during the first two days of the campaign. From the record of pollen in the air in the city concerned, it was evident that no general benefit was obtained by the campaign. During one season \$165,000 was spent on weed destruction in one of our large cities with no appreciable effect on atmospheric pollen contamination. It is only fair to note, however, that in certain areas favored by natural barriers to pollen a judicious expenditure of money might result in effective control of air-borne ragweed pollen.

5. The effective range of pollen depends first on the acreage of the field from which it comes, the stage of development of the pollinating weeds, and such weather factors as rainfall, wind velocity and wind-direction. One may be removed as much as 5 or 10 miles from any large area of ragweeds and still encounter large amounts of pollen dropping from the upper air. Tests have been made 30 miles from shore over Lake Michigan, where it was found that the atmospheric contamination was 75 per cent as much as was found at the same levels and at the same time over the adjacent land. Communities in wooded areas removed as much as 100 miles from agricultural areas enjoy freedom from atmospheric contamination of ragweed pollen when the wind is favorable, but when strong winds blow directly from the agricultural areas the air of such communities may be contaminated with more than enough pollen to cause symptoms in ragweed sensitive persons. It must be remembered that because of convection currents the concentration of pollen in the upper air is fairly constant from the ground to heights of from 4,000 to 6,000 feet.

CONVULSIONS AND HIRSUTISM: DIAGNOSIS

To the Editor:—A woman aged 30 has had attacks of convulsions for the past five years limited to the legs and lasting from twenty to sixty minutes. She also has the feeling that her tongue is large and dry and will block her throat. She feels an attack coming on for many hours before it arrives. She had seven or eight attacks in the first two weeks, following which she was free from them for four or five months. During the attacks she lost 10 to 15 pounds (from 4.5 to 7 Kg.). She has a moderate degree of hirsutism; the thyroid gland has enlarged and she now has a medium sized goiter. After thorough examination, including examination of the nervous system and the blood sugar and the Wassermann test, the diagnosis of epilepsy was suggested but treatment gave no results. The administration of parathyroid extract and calcium was effective: the attacks stopped and the patient gained weight and felt better. Every time she stops, the attacks reappear. The administration of iodine did not influence the illness. Although the attacks are less frequent and the convulsive movements are slight, they come more quickly and the patient seems to be psychologically affected. At present she is receiving parathyroid extract and calcium twenty days a month and iodine the other ten days. Any suggestions for further study or treatment would be appreciated.

M.D., Quebec.

ANSWER.—The patient described presents an interesting but confusing diagnostic problem. The regional convulsions suggest a lesion in the brain. Further evidence for this may be found in the difficulty in swallowing, and the sense of choking from blockage in her throat. Although there is an aura of presentiment long before the attack there is no loss of consciousness that might be expected if this were typical epilepsy. Calcium is a definite though mild sedative, and hence the improvement that the patient obtained from the use of calcium is not necessarily specific.

Among conditions that should be considered are (1) adenoma of the pituitary gland, (2) tumor of the adrenal gland (suggested by the hirsutism), (3) gastric tetany with achlorhydria and faulty absorption or utilization of calcium, (4) idiopathic hypoparathyroidism and (5) primary brain tumor.

There is a considerable literature on each of these conditions. While not entirely typical or pathognomonic of any of them, the symptoms described could be caused by any one of these conditions under certain circumstances. Additional studies that should be made would include:

1. Determination of the blood serum calcium and phosphorus. Consistently high blood serum calcium and low inorganic phos-

phate would suggest an adenoma of a parathyroid gland. Blood calcium of less than 9 mg. per hundred cubic centimeters or higher than normal phosphorus would suggest hypoparathyroidism.

2. A dextrose tolerance test, since the utilization of dextrose is definitely disturbed in some cases of pituitary adenoma or adrenal tumor.

3. Determination of the gastric acidity.

4. Roentgenograms to show the sella turcica.

If the results are compatible with a presumptive diagnosis of adrenal tumor, the adrenal glands may be visualized by injecting air in the perirenal space just before taking a flat plate roentgenogram of this region. Without any evidence of hyperthyroidism, such as would be indicated by a higher than normal basal metabolic rate, iodine medication would seem to be contraindicated, since the large goiter may be largely colloid and cystic, producing less than the normal body requirement of the internal secretion of this gland rather than in a state of hyperactivity. The combination of parathyroid extract and calcium may be merely affording palliative relief from the effects of an organic lesion which should be located and identified.

INSOMNIA AND BAROMETRIC PRESSURE

To the Editor:—An attorney, highly intelligent and honest, states that for several years about twenty-four to twenty-eight hours before a rain he has severe insomnia, which he has at no other times. I have tested him and he predicts a rain accurately every time. Have you any suggestions?

DAN TUCKER MILLER, M.D., St. Louis.

ANSWER.—Many people, as well as wild and domestic animals, exhibit this increased excitability and irritability of the nervous system as low pressure storm centers are approaching and the air temperature and humidity rising. Susceptible persons often awaken in the quiet of the night for no apparent reason other than a sudden fall in barometric pressure. Little is known of the physiologic changes behind these disturbances in central nervous system function. There are hints that a real tissue swelling occurs as outside pressures are reduced and the cells imbibe free water from their surrounding medium (much as does a sponge). Many people have a severe headache, which is relieved as soon as the pressure begins to rise again. Some others with sclerotic changes exhibit a distinct tendency to convulsions and unconsciousness during periods of rapidly declining pressure.

Close investigation under carefully controlled conditions is needed in this field, for violent fluctuations in central nervous function do seem to come with the storm pressure changes. No way has yet been suggested for obviating these pressure disturbances in susceptible individuals; in truth, no such studies have even been undertaken. Petersen's volumes on "The Patient and the Weather" indicates somewhat the direction such studies should take, although they do not answer the question at issue. The only direct therapeutic suggestion to be made is that people thus susceptible to weather changes carefully abstain from central nervous system excitants, of which the most effective in common use is caffeine.

ELECTROCARDIOGRAPHIC LEAD 4 F IN CORONARY THROMBOSIS

To the Editor:—What are the diagnostic electrocardiographic features of lead 4 F in cases of coronary thrombosis? M.D., Arizona.

ANSWER.—If lead 4 F is taken with the polarity recommended by the special committee of the American Heart Association, that is, so that upward deflections in this lead represent positivity of the precordial electrode, the changes that are diagnostic of anterior myocardial infarction are as follows:

Soon after the thrombosis takes place definite elevation, of the S-T segment, usually 3 mm. or more, appears. This upward displacement is due to acute muscle injury and ordinarily disappears within a period of from two to three days after the occlusion. Before the S-T junction has returned to the isoelectric line, inversion of the T deflection at the end of the elevated plateau usually begins to occur and after from a week to ten days large sharply inverted T waves are present. The inverted T waves may persist for several months but eventually disappear.

In addition to these changes in the final ventricular deflection, important alterations in the QRS complex are seen with anterior infarction. The initial upward or positive deflection seen normally in lead 4 F disappears and the entire QRS group may consist entirely of a downward (Q) wave. This type of change is usually present when the infarct is large. If the infarct is small or if the apical lead is close to the edge of the infarct,

W shaped QRS complexes may be found. The modifications of the QRS group are due to the loss of functioning muscle in the heart and are, as a rule, permanent.

It should be emphasized that the changes in the precordial lead just outlined are caused by infarction of the anterior wall of the heart. Infarction of the posterior wall produces no characteristic QRS changes in such leads. In the early stages S-T segment depression is seen, and this finding, if marked, may be of diagnostic help. Later on large sharply upright T waves appear. Chest leads are obviously of limited value when posterior myocardial infarction is present.

BACKACHE SYNDROME: OBER'S SIGN

To the Editor:—Please explain the occurrence of Williams' and Ober's eponymic signs with relation to pain low in the back. If the original source is available, please give the reference.

HAROLD F. ROBERTSON, M.D., Philadelphia.

ANSWER.—Williams did not originate a specific sign or test as an aid to diagnosis of lesions causing pain low in the back. He has accurately described the symptoms and has evolved a logical theory which offers an explanation of the symptoms of the backache syndrome. He believes that the etiology of the lumbosacral and sciatic pain may be found in the degeneration or destruction by injury or disease of the intervertebral disk between the fifth lumbar vertebral body and the sacrum. This results in settling of the fifth lumbar vertebra on the sacrum, with a transfer of body weight back to the articular facets, which may subluxate, narrowing the foramina through which the fifth lumbar nerve roots emerge.

Most of the patients described by Williams have an exaggerated lumbar curve, a sacrospinalis muscle spasm and a fixed downward tilt of the pelvis. Ober's sign is positive when this fixed pelvic obliquity is associated with, if not actually due to, a shortened iliotibial band.

A description of Ober's sign and of the diagnostic observations reported by Williams may be found in the following references:

Williams, P. C.: Lesions of the Lumbosacral Spine, *J. Bone & Joint Surg.*, 19: 343-363, 690-703 (April) 1937.

Ober, F. R.: The Role of the Iliotibial Band and Fascia Lata as a Factor in the Causation of Low-Back Disabilities and Sciatica, *ibid.* 18: 105-110 (Jan.) 1936.

TRANSMISSION OF SYPHILIS

To the Editor:—Many cities now require that food handlers, beauty parlor operators, barbers and others have a certificate from a physician stating that they are free from any contagious or infectious disease, including syphilis. A patient who was treated for syphilis ten years ago with three courses of arsenic and mercury now has a positive blood Wassermann test, a positive spinal fluid and a paretic colloidal gold curve. Neither the wife nor the two children have any evidence of syphilis. Can I fill out the required blank and is there any possibility of the patient's transmitting syphilis?

M.D., Illinois.

ANSWER.—It is not likely that a person who has had syphilis for ten years could transmit it to another person either through sexual intercourse or by any professional act in the food handling or beauty parlor occupations. It would therefore be perfectly permissible, so far as syphilis is concerned, to sign a certificate that the patient is free from any contagious or infectious disease. Such regulations as those cited, singling out food handlers, beauty parlor operators and barbers, with the requirement that they be free from syphilis, is an excellent example of misguided public health hysteria.

IRRADIATION FOR HYPERTHYROIDISM

To the Editor:—What is the status of the application of radium to the neck for the cure of toxic goiter? Has it been used much with good results?

E. C. BAYLEY, M.D., Lake City, Minn.

ANSWER.—In disorders of the thyroid gland it is customary to consider the application of radium and the use of x-rays as the same form of treatment; namely, irradiation therapy. In certain instances, such as toxic adenoma, radium is thought to be superior to the x-rays, but in toxic goiter and hyperthyroidism the results by the two methods are fairly comparable.

Menville (*Radiology* 18:568 [March] 1932) reports data collected from thirty-eight states and seventy-five radiologists. The average of these results show 66.22 per cent of the patients cured and 21.07 per cent improved. Other reports show as high as 90 per cent of cures. Cure, according to Menville, means complete freedom from symptoms for a year following the cessation of therapy. One report (Groover, T. A.; Christie, A. C.; Merritt, E. A.; Coe, F. O., and McPeak, E. M.: Roentgen Irradiation in the Treatment of Hyperthyroidism, *The*

JOURNAL, May 25, 1929, p. 1730) reports that 97.37 per cent of the patients were either cured or markedly improved.

In a recent review of the subject, Jenkinson points out that the percentage of cures remains the same but that fewer patients are reporting for irradiation. He believed this to be due to the improvement in surgical technic until he found that fewer patients were being subjected to surgery in the larger clinics. It would seem that hyperthyroidism is, at least temporarily, on the wane.

The results of irradiation reported by radiologists certainly compare favorably with the results obtained by any other method. It should be remembered that the results obtained by irradiation are more time consuming than those obtained by surgery and, in addition, that the application of radium for this purpose is a highly technical procedure and should not be undertaken by any one who is not thoroughly familiar with the method.

POSSIBLE LEAD POISONING FROM TOOTH PASTE TUBES

To the Editor:—On examination of tooth paste tubes, an oxide of lead is noted to the extent of discolored tooth paste ejected from the tube. When the lining is rubbed with a clean cloth, black oxides are found on the cloth. Would it be possible for a patient who is exposed to these oxides over a long period of time to contract lead poisoning? A tube with a lining prepared by a celluloid varnish which consists of amyl acetate and equal parts of acetone and celluloid prevents this oxide from penetrating the paste.

H. L. KERR, M.D., Crane, Mo.

ANSWER:—If the tube in which tooth paste is enclosed is made of lead, there may be a small amount of lead dissolved in the paste (Danckwortt, P. W., and Siebler, G.: *Zur Toxikologie des Bleis und seiner Verbindungen: III. Bleihaltige Zahnpasten, Arch. d. Pharm.* 265:424-426 (May) 1927). If the tube is tin lined, or otherwise adequately protected, there is no lead absorption by the paste. It is possible that some such technic as that suggested might work effectively. However, one cannot be sure that the "discolored tooth paste" referred to is due to a contamination of lead unless it is so shown by chemical analysis. The amounts of lead found in tooth pastes by Danckwortt and Siebler were not large, and when one thinks what small quantities of tooth paste are used it appears most unlikely that a toxic amount could be obtained from this source. Most tooth pastes are now put up in tin lined tubes.

SENSATION IN ULNAR NERVE FROM IRRIGATION OF SINUS OR FROM MULTIPLE SCLEROSIS

To the Editor:—A man had a mild retrobulbar neuritis, diagnosed by characteristic changes in the visual fields; a chronic bilateral ethmoiditis seemed to be the cause. A submucous resection and left middle turbinectomy was done. As part of the after-treatment, the nose was irrigated with warm saline solution. The patient states that while the nose is being irrigated there is a sensation of warmth in the right arm along the course of the ulnar nerve, from the elbow to the wrist. The first time the nose was irrigated he thought that some of the solution was leaking and running down the forearm, because the temperature felt the same as that of the solution in the nose. Can you explain this phenomenon? Before the operation he complained of occasional numbness and dull pain in both arms and legs. This, however, has now subsided.

E. CLARENCE KERN, M.D., Montclair, N. J.

ANSWER:—There is no generally accepted explanation to account for the sensation of warmth in the right arm along the course of the ulnar nerve from the elbow to the wrist when the nose is irrigated. A possible pathway for such a reflex would be through the fifth nerve from the nose, down the descending branch to the level of the eighth cervical segment and out along the eighth cervical root to the inner side of the forearm. So far as is known, however, no such reflex phenomenon has ever been described. A much more simple explanation would be based on direct pressure on the ulnar nerve by the patient on the arm rest of the chair during the process of irrigation, setting up a mild phenomenon such as is commonly spoken of as one's arm "going to sleep."

The history of the case, however, suggests there may have been a mistaken diagnosis. Retrobulbar neuritis, particularly in a young person, is often the first symptom in multiple sclerosis and is seldom the result of ethmoiditis. Occasional numbness in both arms and legs, plus the sensation complained of along the course of the ulnar nerve, would be consistent with a diagnosis of multiple sclerosis. Other signs, such as changes in the deep reflexes, loss of abdominal reflexes, a history of some dysfunction of the vesical sphincter or attacks of unexplained fatigue should be sought. The finding of a first zone reaction in the colloidal gold test of the spinal fluid would be an additional factor pointing toward a diagnosis of multiple sclerosis.

BODY ODOR

To the Editor:—A professional man, aged 64, always in good health, with normal blood, urine, blood pressure and serologic reaction, has not had the slightest trace of perspiration odor until recently. He was one of those fortunate persons who literally never needed to take a bath, although, being of cleanly habits, he bathed frequently. For several years he has had a senile tremor which is not parkinsonian in character. In the last two months he has been troubled by a peculiar penetrating body odor. This is not noticeable in any particular region; it is subtle and not particularly unpleasant but hard to describe. It is possibly like burned bacon or sulfur. The patient is much troubled about his condition; he is a national figure, and although accustomed to meeting people he is now afraid to because of it. The basal metabolism is normal, there is no hyperhidrosis and the condition seems to be a pure bromidrosis. Have you any suggestions?

M.D., Illinois.

ANSWER:—Bromidrosis is defined as a fetid or foul smelling perspiration. It may be localized or generalized and is usually associated with hyperhidrosis. This case does not seem to show these characteristics. Assuming that the odor has been noticed by the physician and is therefore not an olfactory neurosis, is it strong enough to force itself to the attention of those not especially looking for it? The fact that the patient fears to meet people because of the odor suggests a neurotic state or obsession, and every effort should be made to overcome this fear. If it is an obsession neurosis, the following is suggested: explanation of the mechanism of obsession—that is, false interpretation of a normal sensation; encouragement of daily bathing; some sedative like sodium bromide to be taken twice a day. Examination of the blood is also suggested. It is possible that a 1 or 2 per cent solution of salicylic acid in alcohol as a sponge to the axillae and feet and after bathing a talcum powder containing salicylic acid would help. In view of the fact that the odor "is not particularly unpleasant," it might be possible for an expert in perfuming to make up a perfume for the powder which would cover the odor.

EFFECTS OF LIGATION OF SPLENIC ARTERY

To the Editor:—A white woman aged 64 was operated on for a large cyst of the tail of the pancreas. During the difficult delivery of the base of the cyst, the splenic artery was injured and had to be ligated proximally and distally. The patient made an uneventful recovery. What is known about early or late effects of ligation of the splenic artery?

M.D., Panama.

ANSWER:—The effect of ligation of the splenic artery is the same as the effect of splenectomy. Complete atrophy of the organ will take place, as the splenic artery is the sole arterial supply. In the absence of the spleen other organs assume some of its functions with practically no harm to the individual. Wiggers (Physiology in Health and Disease, ed. 2, Philadelphia, Lea & Febiger, 1937, p. 335) states that splenectomized human beings "live with a more limited reserve, i. e., they are less likely to survive acute hazards of everyday existence which involve decrease in oxygen supply."

BISMARSEN IN SECONDARY SYPHILIS

To the Editor:—A white woman, aged 23, began treatment for syphilis early in the seropositive phase of the secondary stage. She has received continuous treatment to date consisting of seventeen intravenous injections of neoarsphenamine (0.6 Gm.) and twenty-one injections intramuscularly of bismuth salicylate in oil (2 cc., or 0.12 Gm. of bismuth). She has just completed a course of bismuth injections and the blood Wassermann reaction is now negative. I have found it increasingly difficult to introduce neoarsphenamine into her veins and feel that I must use some other method if arsenic therapy is to be continued in her case. Will bismarsen solve my problem? How often should it be administered intramuscularly and how long can it be so administered safely? Is it unwise to allow a rest period of four weeks at this time before I continue with intramuscular therapy in the form of bismarsen? M.D., Pennsylvania.

ANSWER:—No mention is made of how long the blood Wassermann reaction of this patient has been negative, nor is any mention made of results of examination of the spinal fluid after lumbar puncture. One would be in a far better position to advise if these data were furnished. The Cooperative Group has recommended a minimum of twenty injections of an arsenical and of a heavy metal preparation given in continuous form of administration for secondary syphilis. If the lumbar puncture is negative, it might be recommended that the patient be given intramuscular injections of bismarsen, an initial dose of 0.1 Gm. in 1 cc. of sterile distilled water with two or three drops of 2 per cent solution of butyn and then 0.2 Gm. of bismarsen prepared similarly twice a week for the succeeding twenty weeks, this to be followed by a succeeding course of injections of bismuth subsalicylate, and then a repetition of both of these courses. If the blood Wassermann reaction continues to remain negative, it might be safe merely to keep the

patient under observation, a blood Wassermann test being made every three months for the first year and thereafter every six months for two years. There should be a searching physical examination at the discontinuance of therapy, including a cardiovascular check-up. The patient should be examined carefully every year thereafter. If the patient is married, she should of course receive continuous alternating courses of arsenicals and of bismuth throughout each pregnancy.

HEADACHES AND HYPOGLYCEMIA

To the Editor:—A man who seems to be suffering from hypoglycemia has headaches which come on a short time before meals. They are relieved to a certain extent by the use of sugar or other easily assimilated carbohydrates. The sugar tolerance curve parallels normal at a lower level. The headache was relieved by a hypodermic injection of 0.5 cc. of ergotamine tartrate, which was tried as a diagnostic measure. Do you have any information to assist in working out this case or in successfully treating it?

M.D., Calif.

ANSWER.—There is not sufficient detailed information in the query to form a basis for specific suggestions. In general the diagnosis of spontaneous hypoglycemia as a cause of symptoms must be based on the finding of an abnormally low blood sugar level at the time of the symptoms, and the relief of those symptoms by the administration of carbohydrate. The dextrose tolerance curve and the hyperglycemic response to administration of epinephrine have also been used as criteria, but the results of these tests are too variable to be conclusive (Lukens, F. W., and Ravdin, I. S.: *Am. J. M. Sc.* 194:92 [July] 1937). The relief obtained from the administration of ergotamine tartrate is not especially helpful unless one can show that this relief is obtained without the increase in blood sugar which often follows its administration.

The rather constant low blood sugar levels found in endocrine disturbances, such as Simmonds's disease and Addison's disease, rarely are accompanied by characteristic hypoglycemic symptoms. Hypoglycemia due to liver disease is more fluctuating and is more apt to cause symptoms (Judd, E. S.; Kepler, E. J., and Ryncarson, E. H.: *Am. J. Surg.* 24:345 [May] 1934). Hyperplasia, adenoma or carcinoma of the islet cells of the pancreas causes hypoglycemic symptoms but cannot be distinguished from liver disease unless other evidence of liver deficiency or of abdominal tumor is obtained.

Although other methods have been advocated, the most effective medical treatment for hypoglycemic symptoms appears to be a high carbohydrate diet with frequent feedings. If this treatment is not effective, if endocrine disease can be ruled out and liver disease is not apparent, and if the severity of the symptoms warrants it, an exploratory laparotomy is indicated.

DOUCHES AFTER MENSTRUATION

To the Editor:—What is the attitude of the medical profession toward young girls who are virgins taking a douche after every menstruation? This question arose in a physical culture class in a college and I could not say what the doctors in general practice or the gynecologists would say on the matter.

M.D., Massachusetts.

ANSWER.—There is absolutely no justification for advising young girls who are virgins to take douches after menstruation. First of all it is entirely unnecessary and secondly it may result in injury in some cases and masturbation in others. The vagina is perfectly capable of cleansing itself of menstrual blood without artificial aid. Even for women who are not virgins there is no necessity to take douches except for some specific reason.

LYMPHANGIO-ENDOTHELIOMA AND HYPERNEPHROMA

To the Editor:—I recently operated on a boy aged 11 and removed a tumor about 6 cm. in diameter from the second left intercostal muscle. The pathologic report was hypernephroma. Twenty months previously the same child was operated on and a tumor mass removed from the left triceps muscle. The pathologic report of that tumor was lymphangio-endothelioma. The patient has no subjective or objective urinary manifestations which might lead one to suspect any adrenal or kidney involvement. Are these two types of tumors related in any way and may one have a hypernephroma with no involvement of the kidneys or adrenals, such as may arise from adrenal rests?

JOSEPH D. ROMINO, M.D., Fairmont, W. Va.

ANSWER.—Lymphangio-endothelioma and hypernephroma are in no way related, although it is possible to confuse the two histologically in atypical cases. Adrenal rests are not as common as has been generally supposed. Lubarsch found eight adrenal rests in the kidney in 300 necropsies. It is difficult to find any authentic reports of hypernephroma arising in adrenal rests outside the kidney.

ARTIFICIAL MENOPAUSE AT 51?

To the Editor:—A woman in her fifty-first year is menstruating regularly, observing closely a twenty-eight day schedule. Physical examination is negative. She is in good health, and admits it. Is it considered good practice to give this patient a series of irradiations in order to stop menstruation?

M.D., Kansas.

ANSWER.—There appears to be statistical evidence that women who have a late menopause are more likely to develop adenocarcinoma of the body of the uterus and also carcinoma of the breast than women who cease menstruating before the age of 50. Hence some gynecologists and surgeons believe that a late menopause, especially after 50, is a warning of a tendency to malignancy and that adequate treatment should be given to stop the aberrant endometrial activity. Since at the present time this can be accomplished satisfactorily only by means of radium, roentgen rays or operation, it is inadvisable as a routine procedure.

DILATATION OF INTESTINE BELOW OBSTRUCTION

To the Editor:—Can dilatation of the intestine below an obstructive lesion be adequately explained on a physiologic basis? I had such a case recently in which the obstruction was due to postoperative adhesions in an adult. The question arose as to whether or not we were dealing with a megacolon, since the part of the intestine presenting the dilatation was the sigmoid and rectum. However, a biopsy showed no thickening of the bowel wall.

M.D., Illinois.

ANSWER.—There is no physiologic basis for a dilatation of the intestine below an obstructive lesion. If a stricture or continued spasm of the rectum can be ruled out, the most likely diagnosis in this case is a megacolon.

SEXUAL EXCITEMENT AND NERVOUS SYSTEM OF WOMEN

To the Editor:—Does lack of sexual excitement and orgasm have any effect on the nervous system of a normal woman who is menstruating regularly? On that of a normal woman who is not menstruating and who is going through the menopause? What is the best treatise in short form on such matters?

M.D., South Carolina.

ANSWER.—A large number of women go through their entire lives without experiencing any sexual excitement or orgasm. These women may bear children just as do other women and their general health may be good. Many physicians claim, however, that sexual satisfaction is important for the complete physiologic and nervous adjustment of women. Lack of libido probably has no deleterious effect on women who are in the menopause. Interesting books on this subject are those by:

Dickinson, R. L., and Beam, Lura: *A Thousand Marriages*, Baltimore, Williams & Wilkins Company, 1931.
Stekel, Wilhelm: *Frigidity in Woman in Relation to Her Love Life*, New York, Boni & Liveright, 1925.
Gallician, W. M.: *Sexual Apathy and Coldness in Women*, Boston, Stratford Company, 1928.

PROCAINE HYDROCHLORIDE FOR SPRAINS

To the Editor:—In *THE JOURNAL*, August 13, page 646, appears a query captioned "Injection of Procaine Hydrochloride for Sprains." A physician from California asks "Is it considered good practice to inject procaine hydrochloride into a sprained knee as routine treatment? An osteopath nearby is doing this in order that children may continue to play basketball." The answer categorically negatives the advisability of this procedure. *THE JOURNAL* has repeatedly featured this method, first sponsored by Professor Leriche of Strasbourg. Your Paris correspondent under date of Sept. 20, 1933, in *THE JOURNAL* Nov. 4, 1933, states that the medical profession is indebted to Professor Leriche of Strasbourg for the treatment of sprains by injection of procaine hydrochloride. In *THE JOURNAL* Jan. 13, 1934, page 148, appeared the communication of Dr. Ralph R. Fitch not wholly favorable to the method. This elicited the correspondence of Dr. J. C. Weissman published in *THE JOURNAL*, March 3, 1934, page 714, correcting Fitch's misapplication of the method. Followed by the correspondence of Dr. R. E. Logan (*THE JOURNAL*, April 7, 1934) supporting Weissman. Then again your regular Paris correspondent under date of April 18, 1934, gives a "supplementary report of Leriche's method. The article on immediate treatment of articular traumas, by Arnulf and Frieh (*Presse méd.* 42: 597 [April 14] 1934, abstr. *THE JOURNAL* June 23, 1934, p. 2150) confirms Leriche's 1934, abstr. *THE JOURNAL* June 4, 1938, page 1936, contains a lengthy abstract of Professor Leriche's article which appeared in the *Presse médicale* June 12, 1937. Having assiduously followed the teachings of Leriche, may I state that my own experience is wholly at variance with the advice of the commentator. The injection of procaine hydrochloride has been repeatedly applied by me with satisfaction for the relief of painful joint injuries (bandaged or not, splinted or taped) of basketball and football players of the teams of the College of the City of New York, whom I serve in the capacity of surgeon. Equally successful has been its use in the more exacting patients of private practice.

MARTIN W. WARE, M.D., New York.

Medical Examinations and Licensure

COMING EXAMINATIONS

STATE AND TERRITORIAL BOARDS

Examinations of state and territorial boards were published in The JOURNAL, October 1, page 1319.

SPECIAL BOARDS

AMERICAN BOARD OF ANESTHESIOLOGY: An affiliate of the American Board of Surgery. New York, Oct. 21-22. Sec., Dr. Paul M. Wood, 745 Fifth Avenue, New York.

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY: Oral. St. Louis, Nov. 11-12. Sec., Dr. C. Guy Lane, 416 Marlboro St., Boston.

AMERICAN BOARD OF INTERNAL MEDICINE: Written examinations will be held in various parts of the United States, Oct. 17 and Feb. 20. Application for the February examination must be received on or before Jan. 1. Sec., Dr. William S. Middleton, 1301 University Ave., Madison, Wis.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: Written examination and review of case histories of Group B applicants will be held in various cities of the United States and Canada, Nov. 5 and Feb. 4. General oral, clinical and pathological examinations for all candidates (Groups A and B) will be given in St. Louis, May 15-16. Applications must be filed not later than sixty days prior to date of examination. Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh (6).

AMERICAN BOARD OF OPHTHALMOLOGY: St. Louis, May 15. Applications must be filed before February 15. Sec., Dr. John Green, 3720 Washington Blvd., St. Louis.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: Memphis, Tenn., January. Applications for this examination must be filed with the Secretary on or before Oct. 15. Sec., Dr. Fremont A. Chandler, 6 N. Michigan Ave., Chicago.

AMERICAN BOARD OF PEDIATRICS: Detroit, October 26; Rochester, N. Y., November 13; and Oklahoma City, November 15. Sec., Dr. C. A. Aldrich, 723 Elm St., Winnetka, Ill.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: New York, Dec. 28-30. Sec., Dr. Walter Freeman, 1028 Connecticut Ave. N.W., Washington, D. C.

AMERICAN BOARD OF SURGERY: Part I will be given simultaneously in various centers throughout the United States, Oct. 10. Sec., Dr. J. Stewart Rodman, 225 S. 15th St., Philadelphia.

AMERICAN BOARD OF UROLOGY: New York, Jan. 13-15. Sec., Dr. Gilbert J. Thomas, 1009 Nicollet Ave., Minneapolis.

Louisiana June Report

Dr. Roy B. Harrison, secretary, Louisiana State Board of Medical Examiners, reports the written examination held at New Orleans, June 2-4, 1938. The examination covered twelve subjects and included 100 questions. An average of 75 per cent was required to pass. One hundred and fifty-seven candidates were examined, 155 of whom passed and two failed. Eighteen physicians were licensed by reciprocity. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
George Washington University School of Medicine.....	(1936)		78.5
Louisiana State University Medical Center.....	(1937)	78.7, 80.3,*	
(1938)	80.1,* 81.4,* 81.5,* 81.8,* 82,* 82.2,* 82.2,* 82.4,* 82.4,* 82.5,* 82.5,* 82.8,* 82.8,* 82.8,* 82.9,* 82.9,* 83.1,* 83.1,* 83.3,* 83.4,* 83.6,* 83.6,* 83.7,* 83.8,* 84.4,* 84.4,* 84.4,* 84.6,* 84.7,* 84.8,* 84.9,* 84.9,* 84.9,* 85,* 85.1,* 85.1,* 85.1,* 85.1,* 85.4,* 85.5,* 85.7,* 85.8,* 85.8,* 85.8,* 85.9,* 86.3,* 86.4,* 86.6,* 86.6,* 87,* 87,* 87.2,* 87.4,* 87.4,* 87.6,* 87.6,* 87.8,* 88.2,* 88.6,* 89.2*		
Tulane University of Louisiana School of Medicine....	(1938)		76.6,
77.4, 77.8, 77.9, 78.9, 79.1, 79.1, 79.2, 79.4, 79.7, 79.7, 79.9, 79.9, 80.2, 80.2, 80.3, 80.4, 80.5, 80.8, 80.9, 81, 81, 81.2, 81.2, 81.2, 81.3, 81.3, 81.3,† 81.5, 81.5, 81.6, 81.7, 82.3, 82.3, 82.3, 82.5, 82.5, 82.5, 82.7, 82.7, 82.7, 82.8, 82.9, 83, 83.1, 83.1, 83.1,† 83.2, 83.3, 83.3, 83.4, 83.4, 83.4, 83.5, 83.6, 83.7, 83.9, 84, 84, 84.3, 84.4, 84.4, 84.5, 84.7, 84.7, 84.9, 85.2, 85.3, 85.3, 85.5, 85.5, 85.5, 85.6, 85.6, 85.7, 85.9, 86, 86, 86.1, 86.5, 86.9, 87.6, 87.6, 87.8, 88.3, 88.4			
University of Minnesota Medical School.....	(1937)		83.2
Duke University School of Medicine.....	(1937)		82.1‡
Meharry Medical College.....	(1919)		†
University of Tennessee College of Medicine.....	(1937)	80.6, 81.6	

School	FAILED	Year Grad.	Reciprocity with
Tulane University of Louisiana School of Medicine.....	(1938, 2)		
LICENSED BY RECIPROCITY			
University of Arkansas School of Medicine..	(1934), (1936)		Arkansas
George Washington University School of Medicine....	(1931)		Maryland
University of Georgia School of Medicine.....	(1936)		Georgia
Northwestern University Medical School.....	(1932)		Missouri
Rush Medical College.....	(1932)		Illinois
University of Illinois College of Medicine.....	(1931)		Mississippi
University of Minnesota Medical School.....	(1937)		Minnesota
Washington University School of Medicine.....	(1926)		Indiana
Creighton University School of Medicine.....	(1936)		Nebraska
University of Pennsylvania School of Medicine.....	(1928)		Penna.

Meharry Medical College.....	(1931)		Tennessee
University of Tennessee College of Medicine.....	(1925), (1931), (1936)		Tennessee
Vanderbilt University School of Medicine.....	(1928)		Tennessee
Baylor University College of Medicine.....	(1930)		Texas
Marquette University School of Medicine.....	(1925)		Wisconsin
* This applicant has received the M.B. degree and will receive the M.D. degree and Louisiana license on completion of internship.			
† Issued temporary permit. License will be granted on completion of United States citizenship.			
‡ Average grade not reported.			
§ License will be issued on presentation of M.D. degree.			

Kentucky June Examination

Dr. A. T. McCormack, secretary, State Board of Health of Kentucky, reports the written examination held at Louisville, June 8-10, 1938. The examination covered eleven subjects and included 110 questions. An average of 70 per cent was required to pass. Eighty candidates were examined, seventy-nine of whom passed and one failed. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
Rush Medical College.....	(1935)		83
University of Louisville School of Medicine.....	(1934)		81,
87, (1935) 80, (1937) 82, (1938) 76, 76, 77, 78, 78, 78, 78, 78, 79, 79, 79, 79, 79, 80, 80, 80, 80, 81, 81, 81, 81, 81, 81, 81, 81, 82, 82, 82, 82, 82, 83, 83, 83, 83, 83, 83, 83, 83, 83, 83, 83, 83, 84, 84, 84, 84, 84, 84, 85, 85, 85, 85, 85, 85, 86, 86, 86, 87, 87, 87, 87, 88, 88, 89, 90			
Boston University School of Medicine.....	(1936)		87
University of Cincinnati College of Medicine.....	(1938)		87
Vanderbilt University School of Medicine.....	(1938)		83

School	FAILED	Year Grad.
University of Louisville School of Medicine.....	(1938)	

Eighteen physicians were licensed by reciprocity and five physicians were licensed by endorsement from May 26 through August 24. The following schools were represented:

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
Howard University College of Medicine.....			Missouri
Emory University School of Medicine.....			Georgia
University of Georgia School of Medicine.....			Georgia
Northwestern University Medical School.....	(1927)		Illinois
School of Med. of the Division of Biological Sciences	(1933)		Illinois
Tulane Univ. of Louisiana School of Medicine (1935), (1937)			Louisiana
Johns Hopkins University School of Medicine.....	(1934)		Maryland
Detroit College of Medicine and Surgery.....	(1929)		Michigan
Wayne University College of Medicine.....	(1938)		Michigan
St. Louis University School of Medicine.....	(1936)		Missouri
Eclectic Medical College, Chicago.....			Ohio
Ohio State University College of Medicine.....			Ohio
University of Oklahoma School of Medicine.....			Oklahoma
Temple University School of Medicine.....	(1936)		New York
Vanderbilt University School of Medicine.....	(1912), (1937)		Tennessee
Medical College of Virginia.....	(1937)		Virginia

School	LICENSED BY ENDORSEMENT	Year Endorsement of
College of Medical Evangelists.....	(1938)	N. B. M. Ex.
Emory University School of Medicine.....	(1936)	N. B. M. Ex.
Harvard University Medical School.....	(1935)	N. B. M. Ex.
University of Pennsylvania Department of Medicine..	(1898)	U.S.P.H.S.
University of Pennsylvania School of Medicine.....	(1933)	N. B. M. Ex.

Hawaii July Examination

Dr. James A. Morgan, secretary, Board of Medical Examiners, Territory of Hawaii, reports the oral and written examination held at Honolulu, July 11-14, 1938. The examination covered ten subjects and included eighty questions. An average of 75 per cent was required to pass. Five candidates were examined, two of whom passed and three failed. One physician was licensed by endorsement on June 1 after an oral examination. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
Indiana University School of Medicine.....	(1937)		85
University of Toronto Faculty of Medicine.....	(1933)		81.3
FAILED			
Chicago Medical School.....	(1935)		70
University of Tennessee College of Medicine.....	(1937)		71.4
Pennsylvania Medical School, St. John's University, Shanghai.....	(1935)		73
LICENSED BY ENDORSEMENT			
College of Medical Evangelists.....	(1937)		N. B. M. Ex.

Book Notices

Hearing: Its Psychology and Physiology. By Stanley Smith Stevens, Ph.D., Department of Psychology, Harvard University, Boston, and Hallowell Davis, M.D., Department of Physiology, Harvard Medical School, Boston. Cloth. Price, \$4.50. Pp. 489, with 166 illustrations. New York: John Wiley & Sons, Inc.; London: Chapman & Hall, Limited, 1938.

A formal review of this work would in all likelihood not do it justice. Nothing quite like it has appeared in English or for that matter in any foreign language. Here the otologist may recognize with full force the invasion of the field of hearing by physiologists, psychologists and physicists; he may see what exact methods, such as audiometry, have added and see what the vacuum tube, borrowed from the radio, has done in the hands of Wever and Bray and their followers to tell the story of hearing. A glance at chapter headings in this work and a comparison with similar material in standard textbooks of otology will make clear what great changes the past few years have brought. Where will one find, in even advanced textbooks on ear diseases, whole chapters devoted to such topics as the nature of the auditory impulse and the sensitivity of the ear, and pages devoted to the nature of pitch, loudness and other attributes of sound as well as to the character of auditory localization? Investigation in the field of hearing dormant for many years now borrows from the purer sciences and takes advantage of advances in what may seem to be unrelated fields. Those men who effected the revolution in medical training in this country thirty odd years ago and who insisted that the future doctor needed the widest type of scientific education are vindicated. How many otologists would have thought a generation ago that to understand why a patient does not hear he would need to remember how to use the logarithmic tables and the calculus of college days? Every earnest otologist must possess this book and read it. It will not remain the last word on its subject; the authors themselves would be the first to admit this, but, such as it is, it is the most significant signpost to the future in the field of audition in many years.

An Introduction to Clinical Perimetry. By H. M. Traquair, M.D., F.R.C.S., Ophthalmic Surgeon, Royal Infirmary, Edinburgh. With a foreword by Norman M. Dott, M.B., Ch.B., F.R.C.S. Third edition. Cloth. Price, \$0. Pp. 320, with 230 illustrations. St. Louis: C. V. Mosby Company, 1938.

Since his Middlemore Essay on perimetry in 1920, Traquair has become the champion and evangelist of the new third dimensional perimetry, which considers defects in the visual field in relation to the size of the stimulus object. This quantitative concept, which considers not only extent but intensity, was introduced by Bjerrum in his study of glaucoma and elaborated by Roenne. The present general acceptance is largely due to the concise and vigorous exposition in Traquair's textbook, which has become recognized as a modern classic in ophthalmology. The present revision maintains the same format as the original edition, but besides changes in the text it contains fifty-six more pages, sixty-three more figures, two additional colored plates and an enlarged bibliography. The new illustrations are principally from clinical records and aptly elucidate and emphasize the subject matter. By his systematic use of a few white test objects, graduated in size, the depth of a visual defect is mapped in the same manner as altitudes are shown by contour lines. Reduced illumination and color testing aid in searching for defects of very slight intensity and for studying the quality of relative defects. The field for red, 10/300 (10 mm. object at 300 mm. distance), should approximately equal that for white, 10/2,000. If this proportion holds, the condition is generally stationary; but if the red field is markedly smaller, the "disproportion" indicates an actively progressive process. If the quantitative perimetric test is repeated from time to time, slight variations in function are readily discerned. The transition between the defect and the seeing field may be gradual or abrupt, that is, the margin of the scotoma may be "sloping" or "steep" a characteristic of proved significance in diagnosis and prognosis. Tobacco amblyopia is featured by the presence of one or two areas of greater intensity within the scotoma. Even in women who may hesitate to admit an excessive use of tobacco, the demon-

stration of these typical "nuclei" enables a diagnosis to be made with confidence. In retinal detachment, the defect for blue is more intense than that for red, producing a true interlacing of the color fields. In glaucoma, the worse the field, the worse the eye. Traquair advises operation even when fixation is threatened, unless the field as a whole is extremely contracted. He diagnoses rhinogenic retrobulbar neuritis only when sinus disease is evident. In his discussion of acute retrobulbar neuritis he includes toxic amblyopia, Leber's disease, neuromyelitis optica and meningo-encephalitis. The perimetry of disorders of the optic chiasm is considered in detail and divided into lesions of the anterior angle, body and posterior angle. He accepts the conclusions of Cushing and Percival Bailey that temporal lobe tumors tend to present the characters of tract hemianopia, the defect appearing in the nasal field of the eye on the side of the lesion. He believes that the sparing of the fixation area in hemianopic lesions is adequately accounted for by the double vascular supply of the nerve elements concerned with the macula in both the external geniculate body and the visual cortex. Traquair utilizes simple, non-mechanical apparatus and stresses the fact that the most important work in perimetry has been done with the simplest instruments. He still holds that the elaborate refinements of the Ferris-Rand instrument have not yet been proved to be of special value in clinical work, while their utilization entails the serious disadvantage of prolonging the time required for examination. The most expert perimetry can be done with a simple arc perimeter of from 250 to 330 mm. radius and a Bjerrum screen for use at 2 meters. The object should be moved from the blind to the seeing area, as the patient's fixation is thus less likely to be deflected. No routine is advised, but a flexible procedure by which the essential character of the field changes are determined with the minimum fatigue to the patient. Quantitative perimetry has shown that the power of recovery in both the photochemical apparatus and the nerve fiber is extremely high. In almost all forms of interference with the visual path, the tendency to recovery on removing the cause is a prominent feature. The volume charms by its simplicity, satisfies by its thoroughness, and every one seriously interested in ophthalmology or neurology should be familiar with its contents.

Yours to Venture: A Book About Your Future. By Robert B. Updegraff. Cloth. Price, \$2. Pp. 214. New York & London: Whitlsey House, McGraw-Hill Book Company, Inc., 1937.

This is an interesting, challenging book. The thesis is well expressed in the title. The author sees about him a changing world in which new values are replacing the old and in which each individual can find or make a niche for himself, provided only he finds out what he can do best, is willing to venture forth on confidence in his analysis of that ability, and prepared to give of his best, including free "sampling" of his ability, for the reward which he desires. The author believes that in order to get what one desires one must first know what that desire is—in his own terms, one must write a "specification" for one's future in definite terms and then go about fulfilling the specification. He divides individuals not into groups of employers and employees or into doctors, lawyers, merchants, mechanics, farmers, vice presidents or advertising managers but into classes characterized by such descriptive terms as "noticers," "finishers," "specification-writers," "organizers," "salvagers," "seers," "crystallizers," "creators," "inventors," "entertainers," "protectors and comforters" and "packagers." This seems to be an attempt to reduce vocational guidance to a relatively simple and practical formula based on the personal characteristics of the individual. This is, of course, the accepted method, but this book puts it in a new and interesting manner. One may not share the author's optimism when he declares, in effect, that there is a ship for every one to venture in and a reward for all who have the courage to venture, but he may still recommend this book as stimulating reading, even though it fails to get down to any especially practical details. It will undoubtedly stimulate the secretion of the "acid of discontent" which is supposed to be the spur to action, and for those who need just that stimulus it will be a good book. For those who already have the discontent but lack the other

qualities for success, the book may serve only to sink them deeper in the morass of despair, because it makes hard things seem too easy. Physicians, after a careful reading of the book, may choose to recommend it to some of their patients who require psychotherapy, but to some other patients they would undoubtedly not wish to suggest it. The self-rating scale which is found on the reverse of the jacket would be disapproved of by many modern mental hygienists on the ground that it favors unwholesome introspection; most persons might use it for their own amusement, amazement, or possibly more serious self analysis, without harm.

Climate and Acclimatization: Some Notes and Observations. By Sir Aldo Castellani, K.C.M.G., D.S.C., M.D., Professor of Tropical Medicine, Louisiana State University, New Orleans. Second edition. Cloth. Price, 10s. Pp. 198, with 17 illustrations. London: John Bale, Sons & Curnow, Ltd., 1938.

Castellani's book, which was first published in 1930, now appears with, as the author states, "some minor alterations and additions." In view of the fact that Castellani has been inspector general of the Italian military and civil medical services during the Ethiopian war—in association with which there has followed his elevation as count of Kisymaio—he has undoubtedly been very busy, certainly too busy to rewrite the book, which, rather sketchy and inadequate in the first place, is still sketchy and inadequate and reflects a ten year lag. One of the real difficulties with books on climate of the type of Castellani's is the limitation of the discussion of climate to the effects of the tropical climate on northern man. It would almost seem that an interest in the effects of the climate of the higher latitudes must await some adventurous son of the tropics exiled to the north. If tropical air is important for life in the tropics, the variable air of the north might seem equally important for life in the tropical zone. Castellani actually recognizes this in his introductory statement: "Chalmers and I, while recognizing the paramount role played by parasites and hygienic conditions, have persistently endeavored to emphasize the fact that climate per se also plays an important part, and recently there have been signs in various quarters tending to show that the importance of climatic factors is again going to be generally recognized." For the physician interested in a cursory survey of the effect of tropical climate, Castellani's book will be of use; actually, however, the advance in meteoropathology has been rapid since the World War and this advance must be followed in the current literature. Unfortunately widely scattered in journals quite divergent in their particular field of interest—physiology, aeronaotics, meteorology, biometrics, engineering—this material is not considered in the new edition. Fortunately an effort has recently been made to assemble a complete bibliography of the entire field by the Committee on Air Conditioning of the American Medical Association, and this bibliography is now available to the interested American investigator.

Die Röntgentherapie. Unter Mitarbeit von Fachgenossen zusammengestellt von Professor Hans Holfelder, o. ö. Professor für allgemeine klinische Röntgenkunde an der Johann-Wolfgang-Goethe Universität, Frankfurt a. M. Paper. Price, 27 marks. Pp. 341, with 265 illustrations. Leipzig: Georg Thieme, 1938.

The present work is the result of a collection of papers given at the yearly postgraduate course at the Institute of Radiology in Frankfurt on the Main. It is presented under the editorship of Dr. Holfelder and gives an interesting view on the modern methods of roentgen therapy as they are practiced in this institute. A valuable article by Engelmann on the microscopic changes of the pathologic and normal cell after the application of the various methods of irradiation distinctly increases the value of the book.

The textbook is divided into two parts. The first division contains, among other contributions, a review of the physical and biologic problems of the modern methods of roentgen and radium therapy. There is also a chapter on the clinical treatment during and after irradiation, on the treatment of the exposed skin and on studies of the erythema of the skin. The legal aspect of damage to the skin is briefly discussed by Holfelder. The contributors are, besides Holfelder and Engelmann, Holfelder's collaborators (Reisner, Weiswange, Teschen-dorf, Toepfner, Engels and Burkin). Based on the saturation method of Pfahler, the workers developed as the result of many years of experience and through studies of the biologic

problems the present method at the institute of high voltage therapy, which consist in decreasing fractional doses with slow increase of the intervals. Examples of the applied rhythm of administration are given by many tables. Numerous photomicrographs illustrate Engelmann's observations on the pathologic and normal cell exposed to short courses and long courses of irradiation. The latter was administered by the protracted fractional method (Coutard). He concludes that the selective power of rays is increased by the time factor and not by the wavelength. He illustrates this factor by mentioning the Choul therapy, which, though employing rather long wavelengths, results in high efficiency when administered over a long period. He furthermore found when comparing the length of administration that though the protracted fractional method does not damage the connective and muscular tissue it nevertheless more readily endangers the bone marrow and endocrine glands than does the short course. Hence the radiologist should select the proper method for each case. Reisner, whose studies on the erythema of the skin are well known by previous publications, emphasizes again the importance of the rhythm of administration and the selected single dose.

The second division gives in detail the method and results in treatment of cancer of the skin, tongue, pituitary gland and breast, and branchiogenic and esophageal carcinoma. This part is closed by chapters on the treatment of thyroid diseases, Hodgkin's disease and bronchial asthma. The results obtained compare favorably with those of other clinics in Europe and the United States. Nothing as yet can be said of Holfelder's recent method whereby he shortens the time of each single sitting by increasing the roentgen minutes to 90 and the milliamperes to 10. He found the short duration of the sitting especially useful for his method of "compressed irradiation," which, in Holfelder's opinion, is necessary for a better effect on the focus itself. Crossfire and tangential administration of rays are further means of avoiding unnecessary damage.

On the whole, the book is a fundamental description of the method of irradiation practiced in the Institute for Radiology in Frankfurt. It is well written and abundantly illustrated with reproductions of photographs and photomicrographs. Though the methods of irradiation in high voltage roentgen therapy are still changing, this book is a valuable aid for every one working in the field. By its suggestion of careful selection of the dose and rhythm of irradiation, more desirable results may perhaps be obtained with minimal injury of healthy tissue.

Physiological and Clinical Chemistry. By William A. Pearson, Ph.C., M.D., Ph.D., Professor and Head of the Department of Chemistry and Physiological Chemistry in the Hahnemann Medical College and Hospital of Philadelphia, and Joseph S. Hepburn, A.M., B.S. in Chem., M.D., Associate Professor of Chemistry and Research Associate in Gastroenterology in the Hahnemann Medical College and Hospital of Philadelphia. Second edition. Cloth. Price, \$5.50. Pp. 467, with 46 illustrations. Philadelphia: Lea & Febiger, 1938.

These authors are well qualified to correlate biochemistry with clinical medicine, and this completely revised edition should prove useful not only as a textbook but also as a reference volume. The subject matter includes physicochemical principles and qualitative methods, a brief survey of organic chemistry and extensive discussion of the lipids, carbohydrates, proteins and enzymes. The chapters on foods and metabolism incorporate the various clinical, chemical and dietary aspects of this subject with a section on food poisoning. The clinical chemistry per se is carefully arranged so that the methods of examination of the various body fluids are arranged in separate chapters, the chemistry of each being discussed fully. There is an extensive chapter on milk and one on water analysis. Although clinical chemistry is not a standard course in most medical schools, such courses, although elective, do exist and this book should serve as a satisfactory reference work for such teaching. A medical student has no difficulty in correlating his pathology with his clinical medicine; clinical pathologic conferences serve that purpose. There is, however, in most curriculums no correlative course for chemistry, and the application of biochemistry to the clinical sciences is dependent, more or less, on the individual professor of medicine. For those sufficiently informed to seek such correlation, this book is especially recommended.

Pocket Atlas of Anatomy. By Victor Pauchet and S. Dupret. Third edition. Fabrikoid. Price, \$4. Pp. 368, with 345 illustrations. New York & London: Oxford University Press, 1937.

The present edition of this deservedly popular little book, though enlarged, is still a pocket atlas. There were 297 illustrations in the first and 325 in the second edition. The new ones show lymphatics, the solar plexus, relations of the thoracic viscera to the chest wall, and so on. The English edition is published by the Oxford University Press and was printed in Edinburgh. The nomenclature conforms with the Birmingham revision of the BNA. An index has been added. As a pocket companion it will always be interesting and will save many a "quart d'heure" which would otherwise be lost.

Tuberculosis Among Children and Young Adults. By J. Arthur Myers, Ph.D., M.D., F.A.C.P., Chief of Medical Staff and Director of Tuberculosis Activities, Lymanhurst Health Center. With chapters by C. A. Stewart, M.D., Ph.D., Clinical Professor of Pediatrics, University of Minnesota, and Paul W. Gessler, M.D., F.A.C.S., Assistant Professor of Orthopedic Surgery, University of Minnesota. An Introduction by Allen R. Krause, M.D., Lecturer in Medicine, Johns Hopkins University. Second edition. Cloth. Price, \$4.50. Pp. 401, with 71 illustrations. Springfield, Illinois, & Baltimore: Charles C. Thomas, 1938.

This edition contains many references to the newer knowledge concerning tuberculosis in the earlier years of life which has been developed since the first edition. Many chapters have been rewritten and others added. The book is divided into three parts, tuberculosis in infancy, in childhood and in young adult life. One chapter of the first part is devoted to recent advances in the knowledge of tuberculosis and the application of this knowledge in diagnosis, treatment and prevention. Another chapter contains a discussion of sensitization and immunity. Each chapter throughout the book is a concise presentation of the essential facts concerning the subject presented, and all phases of tuberculosis occurring in these age periods are ably presented. One chapter of the second part deals with chronic nontuberculous basal pulmonary diseases in childhood. In each part the subject matter of each chapter is at first discussed and at the end a comprehensive summary is given, followed by a list of references. This arrangement makes the book especially valuable for reference. While some of the opinions may be debatable, the book on the whole is a valuable addition to the literature on tuberculosis and should prove useful to all engaged in tuberculosis work.

Das Rheumabuch des Doctor Ballonius nach der Rheumaschrift des lateinischen Textes, Guillelmi Ballonii Liber de Rheumatismo et Pleuritido Dorsali, Paris 1642. Deutsch herausgegeben von Dr. Walter Ruhmann, Spezialarzt für innere Krankheiten in Berlin. Boards. Price, 1.80 marks. Pp. 70. With portrait. Mittenwald: Theophrastus-Verlag Arthur Nemayer, 1938.

This brochure contains a translation into German of the treatise on rheumatism by Ballonius, published in Paris in 1642. Ballonius, a French physician of the seventeenth century, was not the first to describe rheumatism; his monograph, however, is worth while because of the fine description it gives of rheumatic manifestations. The treatise is not an epoch making contribution but ranks well with the many books of the seventeenth century. In addition to Ballonius's paper, the translator gives a lengthy introduction and an index of the classic contributions to rheumatism throughout the ages.

Medizinische Chemie für den klinischen und theoretischen Gebrauch. Von a. o. Prof. Dr. K. Hinsberg, Vorstand der chemischen Abteilung des Patholog. Univ.-Inst., Berlin, und Dozent Dr. Dr. K. Lang, Stabsarzt, Leiter d. physiol.-chem. Abtlg. d. Militärärztl. Akademie, Berlin. Paper. Price, 18 marks. Pp. 458, with 61 illustrations. Berlin & Vienna: Urban & Schwarzenberg, 1938.

This book is a compilation of the methods used in medical chemistry. The authors state that it is not for beginners, an acquaintance with the various methods being assumed. The book is divided into an "inorganic" and an "organic" section. The original reference to each method, as well as a short criticism of the method, is given. A bibliography concerning modifications of the various methods is given at the end of each section. This volume is a good reference book for those interested in the procedures used in the clinical laboratory. Since, however, many chemical methods in medical chemistry are continuously being improved, one finds some of the methods already somewhat antiquated. For example, the preparation of the sample for lead analysis is too long and unduly intricate.

They use carbon tetrachloride as the solvent for dithizone. Chloroform is preferable because it is a better solvent for the dye and the lead dithizone complex is more stable in chloroform.

Lehrbuch der Differentialdiagnose Innerer Krankheiten. Von Professor Dr. M. Matthes. Fortgeführt von Professor Dr. Hans Curschmann, Direktor der Medizinischen Universitätsklinik in Rostock i. M. Eighth edition. Cloth. Price, 30 marks. Pp. 806, with 132 illustrations. Berlin: Julius Springer, 1937.

This edition merits continued praise as an excellent textbook of differential diagnosis. The presentation of the material is simple and well organized and the subjects differentiated appear in the page margins. The photographic illustrations are excellent. It is of interest that the author includes acute leukemia in the differential diagnosis of acute fevers. This is not usual in standard textbooks of medicine. From the clinical point of view the author is probably correct. The subject matter, whether an acute or a chronic disease, is extremely well differentiated. A condition as rare as arteritis nodosa as well as the common cause of headaches is presented. While the references to the literature are rather old, the author has not failed to mention some of the more recent important observations. The references to the American literature on the whole are scanty and in a few instances erroneous. Thus on page 587 Bagen is misspelled; on page 355, Levine and Boss should be Levine and Golden.

The Anatomy of the Domestic Animals. By Septimus Sisson, S.B., V.S., D.V.Sc. Revised by James Daniels Grossman, G.Ph., D.V.M., Professor of Veterinary Anatomy in the College of Veterinary Medicine, The Ohio State University, Columbus, Ohio. Third edition. Cloth. Price, \$12. Pp. 972, with 770 illustrations. Philadelphia & London: W. B. Saunders Company, 1938.

This book is concerned with the anatomy of the horse, ox, dog, pig and sheep, and to this edition has been added a section on the chicken. The book takes up first the skeleton of these domestic animals, then the joints, fascia and muscles, followed by comparative discussions of the digestive system, respiratory system, urinary and genital organs, vascular system, lymphatic system, nervous system and sense organs. It is well illustrated and should be of great use to persons interested in the anatomy of domestic animals. While the previous edition was published twenty-four years ago, the general plan and scope remain unchanged except for the new chapter on the anatomy of the chicken and the large increase in the number of new illustrations.

Kurzes Handbuch der Ohrenheilkunde. Von Dr. Hermann Marx, o. ö. Professor und Vorstand der Universitätsklinik für Ohren-, Nasen- und Kehlkopfkrankheiten, Würzburg. Paper. Price, 46 marks. Pp. 846, with 463 illustrations. Jena: Gustav Fischer, 1938.

In his preface the author states that this book is not written for the general practitioner or the student of medicine, nor is it a reference work for the experienced specialist. It is primarily intended for the beginning otologist and contains more or less what the author has been accustomed to impart to his assistants regarding the practice of this specialty. Its name belies its character somewhat. The title states that it is a short handbook but the work and index comprise 846 pages. There are numerous illustrations, many of them beautifully colored. There are no particular excursions into the new. This textbook comprises the experience of a lifetime of teaching and can be used with great benefit not only by those for whom it was written but by others even more advanced in the specialty. Examination of the references to the literature cited by the author reveals, as has been stated on other occasions, that in the Teutonic countries there is a tendency to ignore nearly all contributions to the literature excepting their own.

Muir's Bacteriological Atlas. Atlas Enlarged and Text Rewritten. By C. E. van Rooyen, M.D., Halley Stewart Research Fellow and Lecturer in Bacteriology in the University of Edinburgh. Second edition. Cloth. Price, \$5.25. Pp. 90, with 83 illustrations. Baltimore: William Wood & Company, 1937.

This book, meant primarily for beginners in medical bacteriology, should be used in conjunction with a good textbook. The text in this edition has been rewritten and twenty-six new colored plates have been added. The illustrations are good and the legends accompanying them excellent. However, an atlas is no substitute for a good set of microscope slides.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Hospitals: Liability for Defective Equipment.—The plaintiff, aged 74 years, underwent an appendectomy at the defendant hospital. A special nurse, employed to attend him after the operation, learned from the anesthetist that the operating physician desired that the plaintiff be given a "tap water" proctoclysis, an instillation of tap water into the lower bowel, drop by drop. Equipment necessary for a proctoclysis consists of a container, a standard or stand which supports the container above the level of the bed, a rubber tube, a rectal drip, a catheter, and a screw clamp placed on the rubber tubing to regulate the flow. The equipment provided for and placed in the plaintiff's room consisted of a container, a rubber rectal tube and a spring clamp. The special nurse secured a standard and attempted to construct out of these articles the apparatus for proctoclysis. She filled the container with hot water and fastened it to the standard. Realizing then that the equipment was inadequate, she placed the end of the rubber tubing on the bed and went out to secure the other necessary articles, having fastened the spring clamp on the tubing to prevent any flow. In her absence the clamp came apart, allowing the hot water to drain from the container through the rubber tubing and onto the plaintiff's bed so that his back and thighs were severely burned. Because of a spinal anesthetic, the plaintiff was insensitve from the waist down and he did not realize what happened other than that he was warm. In an action against the hospital to recover damages for injuries sustained from the hot water burns the trial court gave judgment for the plaintiff, and the defendant appealed to the Supreme Court of Minnesota.

The plaintiff sought to hold the hospital liable on the theory that it furnished a defective spring clamp, which, because of its defective condition, caused the plaintiff's injury. The trial court correctly instructed the jury, said the Supreme Court, that the defendant could not be held liable for any act or omission of the special nurse; the defendant's liability, if any, must rest on the claimed breach of duty in failing to furnish an efficient clamp, resulting in the plaintiff's injury. One who furnishes an instrumentality for a special use or service impliedly warrants the article furnished to be reasonably fit and suitable for the purpose for which it is expressly furnished. The clamp involved in this case and the other articles present in the plaintiff's room were furnished by the hospital to be used for "customarily needed purposes where an important surgical operation has been performed." The arrangement with the hospital, the court thought, could be nothing less than the furnishing of necessary facilities and equipment for the efficient operation of its business. And these must necessarily be furnished for the particular purpose for which they are needed and designed. The hospital, however, strongly urged that this equipment, among which was the defective spring clamp, was not furnished for use in proctoclysis. The effect of that argument, the court observed, was that, since the use made was other than that intended, injuries arising therefrom are not attributable to any fault of the defendant. With that contention, however, the court found itself in disagreement. It is true that a spring clamp is ordinarily utilized in the administration of an enema where the purpose is to allow either a full flow of the solution or to cut it off altogether. On the other hand, in proctoclysis the solution is injected drop by drop, a result that can be had only by the use of a screw clamp which can be adjusted to increase or decrease the flow, or shut it off completely. The important thing as regards the intended use of the clamp is not the general treatment that is given but rather, and only, the particular function of the clamp in any treatment, i. e., to shut off liquid flow through rubber tubing. The defendant hospital, in the opinion of the court, should be held to be aware of the obvious nature of the use of a spring

clamp, which is the stoppage of the flow of a solution through a rubber tube conduit. And this is so irrespective of the particular treatment being given.

There was, in the opinion of the court, sufficient evidence to show that the clamp was discoverably defective. The effect of the verdict in the lower court was to establish the defendant's negligence. From the evidence the Supreme Court was not prepared to say, as a matter of law, that the defendant could not readily have discovered this defect if a reasonable inspection of the clamp had been made. There was some intimation that the injury was caused by the negligent conduct of the nurse. Her negligence, if any, may be considered, the court said, only in relation to the defective clamp. It was on that theory that the case was submitted to the jury, and the jury's verdict resolved that issue in favor of the plaintiff. The nurse, although a trained professional, could reasonably rely on the hospital's furnishing a proper clamp. The court agreed with the defendant that if the article furnished was obviously unfit for the use for which it was furnished and intended and the nurse used it in violation of the usual standards of due care of nursing practice, the defendant would not be liable for any injurious effects therefrom. But, the court said, the defect was not patent. The clamp was furnished apparently ready for use, and it was not the nurse's duty to examine into its mechanical parts for the discovery of possible defects.

The judgment of the trial court for the plaintiff was affirmed. —*Butler v. Northwestern Hospital of Minneapolis (Minn.)*, 278 N. W. 37.

Medical Societies: Expelled Member Must Exhaust Remedies Within Organization Before Appealing to Court.—The Scotts Bluff County Medical Society, a component society of the Nebraska State Medical Association, which in turn is a constituent association of the American Medical Association, early in August 1935 adopted a resolution declaring it a breach of professional ethics for any of its members to contract individually with county or state officials to render medical care to persons on relief. Weyrens, a member of a society who had opposed the adoption of the resolution, subsequently entered into a contract with certain county and state relief officials whereby he agreed to render medical care to relief clients. After the society had notified him that he had violated the resolution, he was present at a meeting in which the matter was considered and admitted that he had broken the rule and argued against applying it. He was then expelled from the society. He made no effort to appeal from the expulsion order to the councilor of the state association of the district in which he practiced or to the Council of the Nebraska State Medical Association, rights that he could exercise by virtue of the by-laws of the Nebraska State Medical Association. Neither did he make any effort to obtain a rehearing from the county society or reapply after the lapse of one year for membership in the county society, as he had a right to do under that society's by-laws. Instead, he petitioned the district court, Scotts Bluff County, to enjoin the society from depriving him of his rights as a member in good standing. The district court dismissed his petition and he appealed to the Supreme Court of Nebraska.

He complained among other things that he had not been given a trial in the expulsion proceedings. As such matters usually go, in such organizations, said the Supreme Court, he had all the trial then asked for or that was necessary. He was present. He admitted the infraction of the rule adopted and argued against applying it. Any other or further trial would be futile and was unnecessary under the circumstances. There are two reasons, continued the court, why the plaintiff cannot be restored by a court of equity to his position as a member of the local society. First: He has not exhausted his remedies by appealing from the order of expulsion. When he became a member of this voluntary, unincorporated society, he assented to the rules governing the society. Before he can have recourse to the court because of his expulsion, he must

comply with the reasonable and uniform rules of that society, provided they do not contravene the laws of the land or offend public policy. As was said by this court in *Crisler v. Crum*, 115 Neb. 375, 213 N. W. 366:

It is a general rule of equity that, when a member of a voluntary, unincorporated association is aggrieved or feels injured at any action taken by the officers or committees of the association, within the scope of their authority and pertaining to its affairs, and where the laws and rules of the association provide a means of redress, he should first exhaust the remedies provided by the laws and rules of the association before applying to the civil courts.

Secondly: The court refused the relief asked for, because no civil or property right of the plaintiff had been invaded by the disciplinary action of the Scotts Bluff County Medical Society. The fact that a hospital in Scotts Bluff had dropped the plaintiff from its staff as a result of the expulsion proceedings and that the plaintiff's ability to increase his income had been reduced by that action did not, in the opinion of the court, constitute any invasion by the society of a civil or property right of the plaintiff. The hospital was not a party to this action but the evidence showed that one of its rules required the members of its staff and physicians serving the patients therein to belong to the county society. The plaintiff knew this rule and took the consequences when he knowingly and deliberately violated the rule set up by the county society. If the hospital chooses it may change its rule. As it now stands, this rule of the hospital results in inconvenience and some loss of income to the plaintiff but this cannot be attributed to the county society as a deprivation of a property right of the plaintiff. The applicable principle, continued the court, is as follows:

"A court of equity will not inquire into the regularity or validity of disciplinary proceedings by a voluntary unincorporated association, not organized for profit, against one of its members, when no civil or property right of such member will be affected."—*Rogers v. Taugier Temple*, 112 Neb. 166, 198 N. W. 873.

For the reasons stated, the judgment of the district court dismissing the plaintiff's petition for an injunction was affirmed. —*Weyrens v. Scotts Bluff County Medical Soc. (Neb.)*, 277 N. W. 378.

Malpractice: Burns Attributed to Faulty Adjustment of Therapeutic Lamp.—The plaintiffs, husband and wife, sued the defendant, a physician, for burns sustained by the wife during a heat treatment administered by a nurse in the defendant's office. The trial court gave judgment for the defendant, and the plaintiffs appealed to the Supreme Court of Washington.

The complaint alleged that the nurse negligently permitted a hot lamp to come in contact with the patient's back by failing to keep proper control over the device. From the evidence it appeared that when the patient called at the defendant's office for a treatment she had with her her 6 year old daughter, who at the request of the patient remained in the room while the treatment was being administered. In subjecting the patient's body to the heat, a lamp, to which was attached a cord plugged into an electric light socket, was moved back and forth over the patient's body. The patient testified that, at the time she was burned, the nurse had been regulating the heat and had treated her for some time. Finally the nurse pulled the electric plug from the socket but continued distributing the heat from the lamp over the patient's body. While she was so engaged, according to the patient's testimony, the office telephone bell rang and the nurse placed the lamp on some portion of the appliance and started to leave the room. As she was going out, the hot lamp dropped on the patient's back, inflicting the burns. The nurse, on the other hand, seemed to place the blame for the accident on the patient's little girl. The girl, however, testified that she had not touched the lamp and that when the accident occurred she was sitting in a chair reading a book. The patient also testified that the child did not touch the lamp. On appeal, the plaintiffs argued that the trial court had erred in instructing the jury that if they found that the accident was occasioned

by the act of the little girl the defendant was not liable, that the instruction given by the trial court withdrew from the jury the question of fact as to whether or not the defendant and his nurse were negligent in leaving the treatment room while the 6 year old child was in there, the nurse knowing that the child was likely to tamper with the lamp during the nurse's absence. But, said the Supreme Court, nowhere was it alleged that the defendant's negligence consisted of failing to watch the patient's 6 year old child and prevent the child from injuring her mother. The plaintiffs' theory of the case was that the nurse made some adjustment in the lamp and started to leave the room and that, because the device was improperly adjusted, the lamp dropped on the patient's back. If the plaintiffs desired, the court continued, to adopt as an alternative theory the story told by the nurse and then contend, contrary to her complaint and all of the testimony introduced in support of her case, that the child had upset the lamp, and that nevertheless the defendant was still liable for negligence on the nurse's part in not restraining the child, certainly the plaintiffs should have asked for a supplementary or qualifying instruction properly presenting this theory of liability on the part of the defendant. Instead of so asking, the plaintiffs simply excepted to the instructions given. Furthermore, it was admitted that the young child was taken into the room where the treatment was administered, at the request of one of the plaintiffs, the patient. The defendant had provided a place for the children of his patients, but the patient, as she testified, was nervous and wanted the child with her. Generally speaking, then, the plaintiffs could not base any claims against the defendant on the act of their own child. If because of the facts of this particular case a different rule might apply, the burden rested on the plaintiffs to see to it that such a question was submitted to the jury under proper instructions. Clearly from the evidence it could not be held, as a matter of law, that the defendant's nurse was responsible for the acts of the child.

The Supreme Court could find no error in the record, and the judgment of the trial court for the defendant was affirmed. —*Chapman v. Locr (Wash.)*, 76 P. (2d) 600.

Society Proceedings

COMING MEETINGS

- Academy of Physical Medicine, Washington, D. C., Oct. 24-26. Dr. Herman A. Osgood, 144 Commonwealth Ave., Boston, Secretary.
- American Academy of Ophthalmology and Oto-Laryngology, Washington, D. C., Oct. 9-14. Dr. William P. Wherry, 107 South 17th St., Omaha, Executive Secretary.
- American College of Surgeons, New York, Oct. 17-21. Dr. George W. Crile, 40 East Erie Street, Chicago, Chairman, Board of Regents.
- American Public Health Association, Kansas City, Mo., Oct. 25-28. Dr. Reginald M. Alwater, 50 West 50th St., New York, Executive Secretary.
- American Society of Tropical Medicine, Oklahoma City, Nov. 15-18. Dr. E. Harold Hinman, Wilson Dam, Ala., Secretary.
- Associated Anesthetists of the United States and Canada, New York, Oct. 17-21. Dr. F. H. McMechan, 318 Hotel Westlake, Rocky River, Ohio, Secretary General.
- Association of American Medical Colleges, Syracuse, N. Y., Oct. 24-26. Dr. Fred C. Zapffe, 5 South Wabash Ave., Chicago, Secretary.
- Association of Military Surgeons of the United States, Rochester, Minn., Oct. 13-15. Dr. H. L. Gilchrist, Army Medical Museum, Washington, D. C., Secretary.
- Central Society for Clinical Research, Chicago, Nov. 4-5. Dr. Lawrence D. Thompson, 4932 Maryland Ave., St. Louis, Secretary.
- Delaware, Medical Society of, Dover, Oct. 10-12. Dr. Allan V. Gilliland, Smyrna, Secretary.
- Inter-State Postgraduate Medical Association of North America, Philadelphia, Oct. 31-Nov. 4. Dr. W. B. Peck, 27 East Stephenson St., Freeport, Ill., Managing Director.
- Omaha Mid-West Clinical Society, Omaha, Oct. 24-28. Dr. J. D. McCarthy, 107 South 17th St., Omaha, Secretary.
- Pacific Coast Society of Obstetrics and Gynecology, Los Angeles, Nov. 30-Dec. 3. Dr. T. Floyd Bell, 400 29th St., Oakland, Calif., Secretary.
- Radiological Society of North America, Pittsburgh, Nov. 28-Dec. 2. Dr. Donald S. Childs, 607 Medical Arts Bldg., Syracuse, N. Y., Secretary.
- Southern Medical Association, Oklahoma City, Nov. 15-18. Mr. C. P. Loran, Empire Bldg., Birmingham, Ala., Secretary.
- Southwestern Medical Association, El Paso, Texas, Nov. 3-5. Dr. Onille E. Egbert, 116 Mills St., El Paso, Texas, Secretary.
- Western Surgical Association, Omaha, Dec. 2-3. Dr. Albert H. Montgomery, 122 South Michigan Blvd., Chicago, Secretary.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1928 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but may be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American Journal of Cancer, New York

33: 499-658 (Aug.) 1938

- Studies in Carcinogenesis: V. Methyl Derivatives of 1:2-Benzanthracene. M. J. Shear, Boston.—p. 499.
- Granulosa Cell Carcinoma: Malignant Ovarian Tumor Associated with Endocrinologic Effects. E. H. Norris, Minneapolis.—p. 538.
- Production of Experimental Cancer of Lung in Mice. M. G. Seelig and E. L. Benignus, St. Louis.—p. 549.
- Hypophyseal Tumors Induced by Estrogenic Hormone. B. Zondek, Jerusalem, Palestine.—p. 555.
- Study of Effect of "Anticancer Preparations" on Malignant Tissues Grown in Vitro and in Vivo. Anna Goldfeder, New York.—p. 560.
- Leukemia Cell Metabolism in Serum of Normal, Immunized and Leukemic Mice. J. Victor and J. S. Potter, New York.—p. 568.
- Low Serum Glucose in Leukemic Mice. J. Victor and J. S. Potter, New York.—p. 578.

American Journal of Diseases of Children, Chicago

56: 235-482 (Aug.) 1938

- Advantages of Adding Apple to Milk Formulas. F. J. Reithel and I. A. Manville, Portland, Ore.—p. 235.
- Phlyctenulosis. L. B. Burgin and H. L. Higgins, Boston.—p. 239.
- Chronic Gaucher's Disease. D. J. Pachman, Chicago.—p. 248.
- Motor Stability in Children with Cerebral Paralysis. R. L. Jenkins and Muriel Lesser, New York.—p. 266.
- *Acute Pyuria Due to Dysentery Bacilli. H. F. Dietrich, Beverly Hills, Calif.—p. 270.
- *Convulsions Complicating Pertussis: Clinical Study. K. Habel and P. F. Lucchesi, Philadelphia.—p. 275.
- Effect of Milk Supplement on Physical Status of Institutional Children: I. Growth in Height and in Weight. Lydia J. Roberts, Ruth Blair, Blanche Lenning and Marguerite Scott, Chicago.—p. 287.
- Striae in Bones of Set of Monozygotic Triplets. L. W. Sontag and G. Comstock, Yellow Springs, Ohio.—p. 301.
- *Basal Metabolic Rate of Young Children with Nephrotic Syndrome. L. E. Farr, New York.—p. 309.
- Cystic Fibrosis of Pancreas and Its Relation to Celiac Disease: Clinical and Pathologic Study. Dorothy H. Andersen, New York.—p. 344.

Acute Pyuria Due to Dysentery Bacilli.—Dietrich encountered five cases of acute pyuria in which dysentery bacilli were isolated from the urine. Four of the cases are reported. It must be assumed that the dysentery organisms reach the urinary tract by the same route followed by the colon bacilli in cases of ordinary pyelonephritis. All the infections occurred in girls. An ascending infection of the urinary tract is suggested by the sex incidence. The symptoms in the cases cited were neither more nor less toxic than the symptoms of a similar infection due to colon bacilli. The recovery without treatment observed in case 1 and the improvement in case 3 prior to treatment suggest that, like a comparable infection due to colon bacilli, pyuria due to dysentery bacilli is usually subject to spontaneous remission. The urine promptly became sterile in two cases after an adult dose of ammonium mandelate. In the third case the occurrence of vomiting necessitated the omission of medication prematurely. Although the urine had cleared noticeably, the recurrence of frank pyuria and the persistence of bacilluria were observed after ammonium mandelate had been discontinued. After a second bout of fever the urine became sterile coincidentally with the administration of methenamine and ammonium chloride.

Convulsions Complicating Pertussis.—Habel and Lucchesi discuss the clinical features peculiar to convulsions occurring in forty-one of 516 patients with pertussis admitted to the Philadelphia Hospital from 1933 to 1936 and attempt to determine the causes and evaluate methods of combating them. The factors predisposing to convulsions included the age (less than 2 years) of the patient, the severity of the paroxysms, the presence of cyanosis, the presence of bronchopneumonia and

congenital defects of the brain. The convulsive state began with a period of somnolence during which the child was irritable when disturbed. The mortality rate for the series was 78 per cent, but for seventeen patients to whom transfusions were given the death rate was 35 per cent. In the majority of cases no specific pathologic change is present in the brain to point to an essential inflammatory cerebral disease as the etiologic agent; there are, rather, changes that may be attributed to an insufficient blood supply and to anoxemia. Clinically, convulsions usually occur in the spasmodic stage of the disease when the paroxysms are severe. This frequently results in venous congestion of the head and neck, with severe anoxemia. In patients having convulsions when pertussis is complicated by bronchopneumonia, cyanosis and inefficient circulation are instrumental in producing cerebral anemia and anoxemia. Since pertussis convulsions are most likely to occur during the whooping stage and to follow a paroxysm, any therapeutic measure that will reduce paroxysms to a minimum may be definitely considered a prophylactic agent. The various vaccines, given subcutaneously or intracutaneously, are advocated by many clinicians, as are also ether in oil (given by rectum), barbiturates and opiates. However, in the authors' experience convulsions have occurred even in patients receiving each of these remedies. They feel that cyanosis is a responsible causative factor; therefore, oxygen should be used early in all cases of bronchopneumonia and in infants having severe paroxysms even in the absence of bronchopneumonia. Once convulsions have begun, barbiturates should be given by mouth, by rectum or by the subcutaneous route. This should be supplemented with an immediate transfusion of whole blood and with the administration of oxygen (by means of a tent rather than by catheter). Tightly bandaging the extremities seems to help in a few cases. Attempts to overcome cerebral anoxemia should also include treatment to decrease the cerebral edema. Concentrated lyophilic normal human serum seems indicated, because theoretically it would dehydrate the cerebral tissue as well as increase the blood pressure and help to overcome vasomotor collapse.

Basal Metabolism in Nephrosis.—Farr performed thirty-four basal metabolism tests on eight children with the nephrotic syndrome. They showed no significant deviation from the expected metabolic rates, with one exception. In this case a slightly but consistently elevated rate was observed.

American Journal of Ophthalmology, St. Louis

21: 843-962 (Aug.) 1938

- Lectures on Motor Anomalies: I. The Physiology of Ocular Movements. A. Bielschowsky, Hanover, N. H.—p. 843.
- Some Problems Encountered in Cataract Surgery. W. W. Gailey, Bloomington, Ill.—p. 855.
- Further Report on Seton Operation in Glaucoma. M. J. Blaess, Detroit.—p. 865.
- *Diet and Vitamins in Relation to Cataract. A. M. Yudkin, New Haven, Conn.—p. 871.
- Glareless Bed Reading and Examining Lamp with Variable Intensity and Placement of Light. C. E. Ferree and G. Rand, Baltimore.—p. 882.
- Studies on Inclusion Blepharitis: I. Clinical and General Observations. L. A. Julianelle and A. C. Lange, St. Louis.—p. 890.
- Use of Cadaver and Animal Eyes for Training and Experience in Surgery. D. B. Kirby and J. P. Macnie, New York.—p. 904.

Diet, Vitamins and Cataract.—Yudkin favors the theory that attributes the formation of cataract to heredity and senility, local changes in the ocular tissue and general metabolic disturbances. There is some evidence to support the hypothesis that a vitamin deficiency may in many cases contribute to the onset of certain degenerative processes and manifestations of senility. It therefore is important to know what part the vitamins play in the maintenance of normal nutrition and health in the middle aged and the senile person (the person predisposed to cataract). Vitamin A plays an extremely important part in adult nutrition. It should be supplied in liberal proportion not only to youth during growth but in the food of the adult as well, if a good nutrition and a high degree of health and vigor are to be maintained. Vitamin B is responsible in part for the stimulation of appetite and "toning up" of the digestive mechanism. Recently it was suggested that it is in some way concerned in the metabolism of carbohydrate in the body. Vitamin G is essential to growth and to normal nutrition at all ages. When the food is poor in vitamin G for any considerable time, digestive disturbances,

nervous depression, general weakness and deterioration of tone and an unhealthy (or "unthrifty") condition of the skin are apt to develop; the incidence of infectious diseases seems likely to be increased, vitality diminished, life shortened and the prime of life curtailed by the early onset of senility. Vitamin C protects against capillary fragility and helps to protect the body from such changes as are characteristic of the aging process. In view of the present knowledge of human nutrition it is advisable that all elderly patients having any signs of early changes in the lens be instructed in nutrition.

American Journal of Physiology, Baltimore

123:281-542 (Aug.) 1938. Partial Index

- Experiments Concerning Possibility That Inulin Is Secreted by the Renal Tubules. A. N. Richards, P. A. Bott and B. B. Westfall, Philadelphia.—p. 281.
- Recovery of Blood-Perfused Mammalian Nerves. Helen Tredway Graham and R. Lorente de No, New York.—p. 326.
- Quantitative Relationships of Calcium and Cephalin in Experimental Thrombin Formation. J. H. Ferguson, Ann Arbor, Mich.—p. 341.
- Effect of Removal of the Superior Cervical Ganglion on Lacrimal Secretion. J. P. Maes, Boston.—p. 359.
- Observations on Water Metabolism in the Desert. E. F. Adolph, Rochester, N. Y., and D. B. Dill.—p. 369.
- Hunger as a Determinant of Conditional and Unconditional Salivary Response Magnitude. G. Finch, Baltimore.—p. 379.
- Changes in Composition of Sweat During Acclimatization to Heat. D. B. Dill, F. G. Hall and H. T. Edwards.—p. 412.
- Similarity of Effects of Adrenalin and Inhibitory Sympathin on Intestinal Motility; Sensitization by Denervation. W. B. Youmans, Madison, Wis.—p. 424.
- Metabolism of Glucose. J. L. Donnelly, Fort Thomas, Ky.—p. 448.
- Variations in Threshold of Auditory Stimuli Necessary to Awaken the Sleeper. F. J. Mullin and N. Kleitman.—p. 477.
- Direct Evidence of Function in Kidney of Early Human Fetus. Gladys Cameron and R. Chambers, New York.—p. 482.
- Heat Exchanges of Man in the Desert. E. F. Adolph, Rochester, N. Y.—p. 486.
- Changes with Age in Renal Function in Adult Men: I. Clearance of Urea. II. Amount of Urea Nitrogen in the Blood. III. Concentrating Ability of Kidneys. W. H. Lewis Jr. and A. S. Alving, New York.—p. 500.
- Rate of Removal of Hemoglobin from the Circulation and Its Renal Threshold in Human Beings. R. Ottenberg and C. L. Fox Jr., New York.—p. 516.
- Effect of Different per Cents of Protein in the Diet in Successive Generations. J. R. Slonaker, San Francisco.—p. 526.

American Journal of Public Health, New York

28:907-1028 (Aug.) 1938

- Mercury Poisoning from Public Health Viewpoint. P. A. Neal, Washington, D. C.—p. 907.
- Public Health versus Public Welfare. H. Folks, New York.—p. 916.
- Health Department in the Field of Medicine: From Standpoint of Private Practitioner. C. H. Goodrich, Brooklyn.—p. 923.
- Chloramine Treatment of Sea Water. L. V. Carpenter, L. R. Setter and M. Weinberg, New York.—p. 929.
- *Measles in Detroit, 1935: I. Factors Influencing Secondary Attack Rate Among Susceptibles at Risk. F. H. Top, Detroit.—p. 935.
- Nutritional Education in the Home: Dutchess County (N. Y.) Project. B. E. Roberts, Poughkeepsie, N. Y.—p. 944.
- Indiana's Dental Health Program. J. B. Mettel and Mary H. Westfall, Indianapolis.—p. 949.
- Plumbing in Low Cost Housing. J. I. Connolly, Chicago.—p. 954.
- Housing and Health. R. H. Britten, Washington, D. C.—p. 957.

Measles.—Top states that 27,430 cases of measles were reported in Detroit during 1935. Follow-up visits were made to every fifth family in which one or more susceptible contacts had not been reported as having developed measles in order to determine the accuracy of the history of previous measles and the number of cases which had not been reported. Analysis of age, sex, relationship of the period in the seasonal cycle to the secondary attack rate, relationship of the number of primary cases (1,253) per family to the secondary (1,380) secondary cases of 1,633 contacts) attack rate, the effect on secondary attack rates occasioned by repeated exposure to a constant intensity and the effect on secondary attack rates occasioned by one exposure to various intensities which might affect the secondary attack rate in a random sample of families resulted in the following conclusions: 1. The sex of the primary patient or that of the susceptible contact is unimportant. 2. Age of the primary patient may exert an influence on the secondary attack rate. Further investigation of this factor would appear desirable. 3. The age of the susceptible contact influences the secondary attack rate significantly. 4. Secondary attack rates are not greatly affected by the period

in the seasonal cycle in which measles first appears in the family. 5. The number of primary cases per family does not affect the secondary attack rate among the susceptible persons in the same family. 6. There is an additional hazard when a contact is exposed to measles a second time. 7. Intensity of exposure as measured by the number of cases in the family at one time does not appear to influence appreciably the secondary attack rate among the susceptible persons.

Am. J. Roentgenol. & Rad. Therapy, Springfield, Ill.

40:165-324 (Aug.) 1938

- Roentgen Kymographic Studies on Aneurysms and Mediastinal Tumors. W. G. Scott and S. Moore, St. Louis.—p. 165.
- Roentgen Kymography of Normal Colon Defecation in Man. R. A. Rendieh and L. A. Harrington, Brooklyn.—p. 173.
- Malignant Bronchial Stenosis: Bronchographic Aspect. P. L. Farías, Havana, Cuba.—p. 180.
- Significance of Left Auricular Dilatation in Auricular Fibrillation. M. L. Sussman and M. T. Woodruff, New York.—p. 184.
- Roentgenologic Examination of Normal Breast: Its Evaluation in Demonstrating Early Neoplastic Changes. J. Gershon-Cohen and A. Strickler, Philadelphia.—p. 189.
- *Resolving Lobar Pneumonia in Adults Simulating Tuberculosis in Roentgenogram. S. Cohen, Jersey City, N. J.—p. 202.
- Roentgenologic Manifestations in Bone Syphilis. D. M. Stewart, Toledo, Ohio.—p. 215.
- Lactie Osteitis Simulating Malignant Disease. A. H. Ungerman, W. H. Vicary and W. W. Eldridge, Washington, D. C.—p. 224.
- Roentgen Findings in Morvan's Type of Syringomyelia. F. B. Mandeville, Richmond, Va.—p. 230.
- Congenital Absence of Middle of Esophagus. A. S. Ungér and M. H. Poppel, New York.—p. 240.
- Effect of Roentgen Rays on Stomach in Rabbits. R. B. Engelstad, Oslo, Norway.—p. 243.
- *Results Obtained in Radiation Treatment of Inoperable Collum Carcinoma. I. de Büben, Budapest, Hungary.—p. 264.
- Factors Influencing Quantitative Measurement of Roentgen Ray Absorption of Tooth Slabs: X. Tissue Factors. H. C. Hodge, G. Van Huysen and S. L. Warren, Rochester, N. Y.—p. 269.
- Advantages of Non-Screen Roentgenography. H. H. Duerr, Binghamton, N. Y.—p. 283.
- Case Report from the Weekly Seminar of the Roentgenologic Department of the Massachusetts Hospital, Boston. J. R. Lingley, Boston.—p. 291.

Resolving Lobar Pneumonia Simulating Tuberculosis.

—Of the various pathologic phases of pneumococcal pneumonia, the stage of resolution from a roentgenologic point of view has probably been least appreciated. The problem of differentiation between some cases of pneumonia and tuberculosis Cohen has encountered ten times; five cases are reported which illustrate especially instructive roentgenologic features of resolution of lobar pneumonia in adults. All had been incorrectly diagnosed at one time or another as tuberculosis. The error committed was that of faulty interpretation and evaluation of the roentgenograms of the chest, particularly of a single film. The points that the author discusses are the pathology of a normally resolving unilobar pneumonia, x-ray appearance of a normally resolving unilobar pneumonia, roentgenologic differentiation between resolving lobar pneumonia and tuberculosis, and factors in delayed resolution. For roentgenologic differentiation between the two diseases, the value of serial roentgenograms taken at short intervals is emphasized.

Radiation Treatment of Collum Cancer.—From 1919 to 1929 de Büben states that 702 cases of inoperable collum carcinoma were treated by irradiation at the Women's Clinic. There were 658 cases with an inoperable condition in which the uterus was fixed and the carcinoma invaded the neighboring tissues and forty-four of highly advanced and hopeless cases of inoperable collum carcinoma. From the standpoint of palliative effect 305 patients, or 43.1 per cent, showed primary healing. From the standpoint of complete cure, on a basis of at least five years with an absence of symptoms, thirty-eight patients were completely cured. According to the usual method of treating inoperable collum carcinoma, tubes containing 25 mg. of radium supplied with a primary silver-brass-lead filter are used. Usually 50 mg. of radium is used; the time of irradiation extends from twenty-four to forty-eight hours. If at all possible the vaginal radium treatment is completed with the intracervical method. For this purpose radium tubes with sterilized containers which are supplied with filters corresponding to a total of 1 mm. of platinum are introduced into the cervical canal after it is dilated. With the combination of the vaginal and cervical

methods, from 4,000 to 6,000 milligram hours is generally used. The treatment is distributed over several weeks. In the advanced cases of collum carcinoma in which the cervix cannot be reached without causing damage to the tissue, only the vaginal method is resorted to and consequently smaller doses of radiation are used than are employed in the combined method.

Archives of Dermatology and Syphilology, Chicago

38: 329-510 (Sept.) 1938

- Value and Limitations of Biopsy in Dermatology. H. Montgomery, Rochester, Minn.—p. 329.
- *Treatment of Pruritus Ani by Tattoo with Mercuric Sulfide. E. Hollander, New York.—p. 337.
- Active Sweat Glands: Method for Their Study. H. M. Buley, Champaign, Ill.—p. 340.
- *Dermatitis and Stomatitis from Mercury of Amalgam Fillings. E. F. Traub and R. H. Holmes, New York.—p. 349.
- Extragenital Granuloma Inguinale. R. B. Greenblatt, R. Torpin and E. R. Pund, Augusta, Ga.—p. 358.
- Trichostasis Spinulosa. E. F. Corson, Philadelphia.—p. 363.
- *Dermatophytosis of the Feet: Sources and Methods of Prevention of Reinfection. D. A. Berberian, Beirut, Syria.—p. 367.
- Sudoriparous Glands: II. Apocrine Glands. S. C. Way, San Francisco, and A. Memmesheimer, Essen, Germany.—p. 373.
- Mouse Brain Lymphogranuloma Venereum Antigen: Clinical Experience at Cleveland City Hospital. G. W. Binkley and W. R. Love, with collaboration of W. F. Schwartz, J. M. Hitch Jr. and Grace A. Margard, Cleveland.—p. 383.
- Dermatologic Symptoms of Vitamin Deficiencies. H. Goodman, New York.—p. 389.
- Lichen Planus of Lips. D. W. Montgomery, San Francisco.—p. 401.
- "Acne Mixed" Undenatured Bacterial Antigen in Treatment of Acne Vulgaris. M. J. Costello and J. C. Washburn, New York.—p. 405.
- Dermatitis Gangraenosa Infantum. M. L. Blatt, C. K. Stulik and A. Nachman, Chicago.—p. 407.
- Relapsing Febrile Nodular Nonsuppurative Panniculitis (Weber-Christian Disease): Report of Two Cases. Loretta Joy Cummins and W. F. Lever, Boston.—p. 415.
- Reliable Method of Staining Spirochaeta Pallida in Smears. A. A. Krajian, Los Angeles.—p. 427.
- Folliculitis Naris Perforans: Report of Case. R. B. Palmer, Lincoln, Neb.—p. 429.

Tattoo Treatment of Anal Pruritus.—Hollander tattooed with mercuric sulfide the perianal skin of fifteen patients for severe chronic anal pruritus. This resulted in the relief of the itching and the return of the skin to a normal texture. Two patients have remained well for more than one year, three for more than six months and ten for less than six months. The duration of the symptoms previous to treatment ranged from two to seventeen years. In none of these cases was any rectal or constitutional disease found to account for the rectal itching. In five of the cases, after repeated scrapings of the fissured skin, segments of mycelium were seen on microscopic examination.

Dermatitis and Stomatitis from Amalgam Fillings.—Traub and Holmes have recently encountered two instances of dermatitis caused by the mercury of amalgam fillings. In the first patient a mild stomatitis was present. Such cases represent examples of contact dermatitis rather than of irritation of the skin and the mucosa resulting from the absorption of mercury from the amalgam fillings. From a review of the controversial literature on the subject of chronic mercurial poisoning resulting from amalgam fillings it is concluded that: 1. The danger to the patient of chronic mercurial poisoning from silver amalgam fillings alone is remote. 2. Chronic mercurial poisoning from copper amalgam is not frequent and is to be expected only in hypersensitive subjects. 3. Acute manifestations such as dermatitis or stomatitis are probably more common than is generally believed. 4. The degree of sensitivity to different preparations of mercury varies in individuals, nor does every person necessarily react to all mercurial compounds. The skin generally reacts more readily to the external application of mercury than does the mucous membrane.

Dermatophytosis of the Feet.—Berberian believes that the stockings of patients with ringworm are the commonest source of reinfection. Not only is the fungus found on stockings of patients suffering from the infection but it survives the ordinary process of laundering and is capable of growing in the fabric. His experiments show that *Trichophyton interdigitale* is capable of growth on different kinds of materials used as inner lining for shoes and also on wood, rock, moss and seaweeds. The use of all rubber slippers in gymnasiums and on beaches is recommended as a means of safeguarding one's feet against the possibility of infection or reinfection from

exogenous sources. The vapor of formaldehyde is an effective disinfectant against *Trichophyton interdigitale*. Its disinfecting action is greater and more rapid (six hours) when the article to be disinfected is moistened just before being placed in the disinfecting chamber.

Archives of Otolaryngology, Chicago

28: 153-312 (Aug.) 1938

- Cancer of Larynx: Immediate and Ultimate Results of Operation in 102 Cases. H. B. Orton, Newark, N. J.—p. 153.
- *Objective Tinnitus Aurium. E. A. Bredlau, Chicago.—p. 193.
- *Bronchial Asthma and Nasal Allergy. M. A. Ramirez, New York.—p. 199.
- Cholesteatoma Verum of Right Mastoid. M. D. Friedman and S. S. Quittner, Cleveland.—p. 209.
- Psychiatric Therapy for Dysphonia: Aphonia; Psychophonesthenia; Falssetto. J. S. Greene, New York.—p. 213.
- Influence of Sulfanilamide on Infected Sinuses of Rabbits: Chemical and Microscopic Studies. B. J. McMahon, St. Louis.—p. 222.
- Fulminating Infection of Nose Due to *Monilia* or *Aspergillus*: Report of Case. C. S. Nash, Rochester, N. Y.—p. 234.
- Recovery of Patient with Type III *Pneumococcus* Meningitis of Otitic Origin. J. Gubner, Brooklyn.—p. 241.
- The Paranasal Sinuses. S. Salinger, Chicago.—p. 252.

Objective Tinnitus Aurium.—Bredlau reports three cases of objective tinnitus and reviews similar cases described in the literature. Objective tinnitus may be either vascular or muscular in origin. Spasmodic contractions of the eustachian tube are the chief causative factors in the muscular type of objective tinnitus; the immediate cause is the separation of the moist surfaces of the eustachian tube. Hysteria and neurasthenia have been hypothesized as predisposing or contributing factors. The vascular type of tinnitus is caused by the preternatural transmission of arterial or venous impulses to the ear by (1) aneurysms, including arteriovenous aneurysms, both intracranial and extracranial, (2) hypertension, (3) vascular tumors of the brain and the ear, (4) coarctation of the aorta, (5) severe anemias, (6) pregnancy, (7) acute inflammatory disease of the ear and (8) vasomotor and endocrine disturbances.

Bronchial Asthma and Nasal Allergy.—Ramirez regards bronchial asthma as a clinical entity and defines it as a bronchial neurocellular syndrome characterized by recurrent attacks of paroxysmal dyspnea. He divides asthma into two large types, (1) broncho-edematous and (2) bronchospastic. The broncho-edematous type, in which there is edema of the bronchial mucosa, includes asthma due to sensitization to an allergen. Truly non-allergic asthma due to remote stimulation by some other excitant, such as a pathologic condition of the nose, the effects of heat and cold or emotion, manifests not broncho-edema but bronchospasm. Therefore in most cases in actual practice the condition is of a mixed type pathologically, even though etiologically it belongs fundamentally to one type. In diagnosis, statistics on heredity in allergy are undependable. There are many pitfalls in sensitization tests. For example, a physician with seasonal asthma had negative reactions to cutaneous, ophthalmic, passive transfer and inhalation tests in the nose. However, he reacted immediately to the inhalation of ragweed pollen directly into the lungs. The average patient requires care from both the allergic and the nonallergic angle. Satisfactory results will not be obtained merely by eliminating offending allergens or by attempts at hyposensitization. The pathologic condition must be corrected surgically. There is no doubt that many patients with sinusal involvement are allergic and should not be operated on. The bronchospastic type of asthma resulting from remote reflex stimuli originating in the nose or the accessory sinuses obviously will not be benefited except by elimination of the local pathologic condition. In cases of broncho-edematous asthma in which sensitization has taken place a gross nasal pathologic condition must be corrected surgically if lasting satisfactory relief of symptoms is to be expected; this, of course, must be in addition to proper treatment from an allergic standpoint. Grains of pollen embedded in the lining membrane of the antrums and possibly of the other sinuses may in this way be responsible for the continuance of symptoms in highly sensitive persons after the particular pollen has disappeared from the air of the locality. The author believes that there is a definite relation of endocrine dysfunction and vitamin

deficiency not only to asthma but to allergy in general. He does not think that any one gland or a deficiency in any one vitamin is solely responsible. Any gland or combination of glands may be an important factor affecting the underlying fundamental mechanism of hypersensitiveness. This phase of allergy indirectly may involve a strong hereditary influence and determine the shock tissue.

California and Western Medicine, San Francisco

49: 105-176 (Aug.) 1938

- Anesthesia in Europe. W. L. Garth, San Diego.—p. 112.
Conservative Renal Surgery, with Particular Reference to Kidney Trauma. L. E. Kindall, Oakland.—p. 115.
Tuberculous Tracheobronchitis: A Review. P. H. Pierson, San Francisco, and P. C. Samson, Oakland.—p. 120.
Roentgen Treatment of Certain Hemorrhagic Disorders. L. H. Garland, San Francisco.—p. 123.
*Vitamin D in Acne: Comparison with X-Ray Treatment. M. T. R. Maynard, San Jose.—p. 127.
Trauma and Malignancy. E. I. Bartlett, San Francisco.—p. 132.
Believe-It-Or-Nots in Urology. W. B. Dakin, Los Angeles.—p. 135.

Vitamin D in Acne.—Maynard reviews 255 cases of acne treated since 1930. Of these, 123 patients were treated by means other than the use of viosterol and 132 with viosterol; eighty-six were treated with the roentgen ray. The dietary instructions and the local applications were identical in the two groups. Of those receiving viosterol the dosage was started at 20 drops each morning; in many the dosage was later increased to 40 drops. The reason for the morning dose was to take advantage of the influence of sunlight on the synthesis of vitamin D in the skin. Of the eighty-six patients treated with roentgen rays the acne was better in thirty at the end of three months, in thirteen it was much better and in twenty-six the condition was healed; and of the 132 patients treated with viosterol the respective numbers were eight, twenty and thirty-two. There were twenty-one relapses in the first group of patients against one in the second group. The percentage of satisfactory results at the end of three months was 48 in the roentgen group and 75.6 per cent in the viosterol group.

Canadian Medical Association Journal, Montreal

39: 105-206 (Aug.) 1938

- Acute Anterior Poliomyelitis: Review of Sixty-Six Adult Cases Which Occurred in the 1937 Ontario Epidemic. H. H. Hyland, W. J. Gardiner, F. C. Heal, W. A. Oille and O. M. Solandt, Toronto.—p. 105.
*Human Response to Single Doses of Sulfanilamide. C. C. Lucas, Toronto.—p. 111.
Pathologic Interpretation of Some Surgical Procedures Adopted for Relief of Glaucoma. F. T. Tooke, Montreal.—p. 114.
Need for Prolonged Artificial Respiration in Drowning, Asphyxiation and Electric Shock. G. Bates, R. E. Gaby and W. MacLachlan.—p. 120.
*Percutaneous Tuberculin Reaction. H. P. Wright, A. F. Chaisson and R. Allison, Montreal.—p. 123.
Cardiac Lesions in Adrenal Insufficiency. G. E. Hall and R. A. Cleghorn, Toronto.—p. 126.
Relation of Pregnancy to Biliary Disease and Control of Vomiting of Pregnancy. J. M. McGowan and J. O. Baker, Quincy, Mass.—p. 133.
Changes in Olfactory Mucosa and Olfactory Nerves Following Intranasal Treatment with One per Cent Zinc Sulfate. C. G. Smith, Toronto.—p. 138.
Large Solitary Cysts of the Kidney: Report of Case. S. A. Wallace, Kamloops, B. C.—p. 140.
Recurrent Intra-Ocular Hemorrhage in Young Adults (Eales' Disease): Report of Case. S. H. McKee, Montreal.—p. 142.
Trial Study of 1,800 Cases of Syphilis Infected Twenty Years Ago. F. S. Burke and Margaret Parks, Ottawa, Ont.—p. 145.
Significance of Epigastric Hernia. J. C. Luke, Montreal.—p. 149.
Points of Mutual Interest to the General Practitioner and the Radiologist. W. A. Jones, Kingston, Ont.—p. 152.
The Psychiatrist's Point of View. J. D. M. Griffin, Toronto.—p. 157.
Value of Correcting Red Cell Sedimentation Rate for the Effect of Cell Volume. D. W. Crombie and A. Hambleton, London, Ont.—p. 162.
Military Tuberculosis in Newborn Infant. G. M. White and D. F. W. Porter, St. John, N. B.—p. 165.
The Department's Responsibility for Food Protection. R. E. Wodehouse, Ottawa, Ont.—p. 167.

Single Doses of Sulfanilamide.—Lucas took 15, 30 and 45 grains (approximately 1, 2 and 3 Gm.) of a commercial sample of prontosil at intervals of about two weeks. The drug was taken for experimental purposes. The drug was taken by mouth, with about 150 cc. of water, one hour after a light breakfast. Samples of blood and total urine were collected for analysis at intervals of one hour for six hours following the ingestion of the drug. The blood was again

examined twenty-four hours after the sulfanilamide was taken. The urine was collected and analyzed after eight, ten, twelve, twenty-four and forty-eight hours. Following the largest dose (45 grains) the forty-eight to seventy-two hour urine was also collected and a final specimen was collected on the fourth day. Only mild ill effects were noted following the ingestion of any of the doses of sulfanilamide. A feeling of considerable fatigue began about six hours after each of the two larger doses was taken but it was not severe enough to necessitate any curtailment of usual activities. Slight hyperesthesia followed the largest dose, about ten hours after the drug was taken, and it was in the form of a mild formication; during the following day a slight tingling sensation about the face and finger tips was present. The concentration of sulfanilamide in the blood was not directly proportional to the dose. Blood concentrations of sulfanilamide above 5 mg. per hundred cubic centimeters are not easily attained (while liver and kidney function are normal), since conjugation and excretion occur rapidly. The proportion of sulfanilamide which undergoes conjugation is not constant.

Percutaneous Tuberculin Reaction.—Wright and his colleagues employed an ointment for the percutaneous test by absorbing old tuberculin with fullers' earth and then adding enough hydrous wool fat to make an ointment. On a quantitative basis, 1 cc. of old tuberculin required 1 Gm. of fullers' earth and 2.25 Gm. of hydrous wool fat. Prior to application of the ointment the skin of the selected site on the chest over the sternum was cleansed with ether and then a small portion of ointment (about the size of half a dry pea), was rubbed into an area about the size of a fifty cent piece (30 mm.). Sixty revolutions with the finger were taken as an arbitrary standard. A rubber finger cot was worn on the finger. Within twelve hours, 73 per cent of forty-four tuberculous patients tested showed pale or pinkish papules, either alone or with surrounding zones of erythema and the skin induration on the site of ointment application. After twenty-four hours there was a distinct reaction in 94 per cent and after forty-eight hours 100 per cent of the patients had reacted positively. The papules, which are a distinctive feature of the skin reaction, varied in number from ten to twelve to more than 100 in different cases. In a general way, those patients who were known to be most allergic from their intradermal tests gave the most marked percutaneous reactions but there were enough exceptions to render this impression only tentative. The percutaneous test was checked in the general medical wards. All patients there receive a Mantoux test as part of their routine investigation. A positive percutaneous reaction was obtained in only three cases, which coincided exactly with the observations on routine intradermal injection of 0.1 cc. of old tuberculin. In all, fifty-seven general ward patients were examined in this manner. A control ointment containing the same amount of fullers' earth and hydrous wool fat but no old tuberculin was also used on all the patients tested in the general medical wards. Two patients with negative Mantoux reactions showed small areas of slight erythema on both test and control sites. These disappeared after thirty-six hours. No papules, which seem to be the distinctive feature of the positive percutaneous reaction, were present. The cheapness of ointment testing, together with its stability, warrants more intensive application of the percutaneous test by physicians and others interested in detecting early cases of tuberculosis in childhood. As a case finder outside hospitals the percutaneous test with tuberculin ointment has a definite field of usefulness.

Canadian Public Health Journal, Toronto

29: 373-424 (Aug.) 1938

- Some Public Health Needs in Nova Scotia: Presidential Address. C. E. A. deWitt, Wolfville, N. S.—p. 373.
Progress in Housing and Health. R. St. J. Macdonald, Montreal.—p. 377.
Cancer in Ontario. A. H. Sellers, Toronto.—p. 387.
The Laughlin Test for Syphilis. G. F. Laughlin, Toronto.—p. 396.
Reallocation of Nonresident Births and Deaths. E. J. Picton, Hamilton, Ont.—p. 401.
Antitoxin Response in Guinea Pigs Deficient in Vitamin C. G. D. W. Cameron, Toronto.—p. 404.

Delaware State Medical Journal, Wilmington

10: 167-188 (Aug.) 1938

- Tuberculosis in Delaware. A. C. Jost, Dover.—p. 167.
Comparative Incidence of Tuberculosis Among the White and the Colored in Delaware. L. D. Phillips, Marshallton.—p. 170.
The State's Crippled Children's Program. W. E. Morris, Dover.—p. 172.
Nemours Foundation for Crippled Children. A. R. Shands Jr., Wilmington.—p. 174.
Pneumonia Control. A. C. Jost, Dover.—p. 177.
The Interstate Commission on the Delaware River Basin: Its Beginnings, Growth and Plans. R. C. Beckett, Dover.—p. 177.
Syphilis in Delaware. T. E. Hynson and J. R. Beck, Dover.—p. 180.
Serodiagnosis: Results in Latest Evaluation Study. R. D. Herdman, Dover.—p. 182.
Study of Kent County Births for the Year 1937. E. F. Smith, Dover.—p. 183.
Housing and Public Health Nursing. Kathryn Trent, Dover.—p. 184.
Dental Hygiene Service for the Expectant Mother and Infant. Margaret H. Jeffreys, Dover.—p. 185.

Illinois Medical Journal, Chicago

74: 97-196 (Aug.) 1938. Partial Index

- Tumors of the Breast. I. Ahell, Louisville, Ky.—p. 119.
Prenatal Care. W. C. Danforth, Evanston.—p. 127.
Anemia and Jaundice in the Newborn. W. M. Whitaker, Quincy.—p. 134.
Feeding of Full Term Infants During the Newborn Period. G. M. Cline, Bloomington.—p. 142.
Pulmonary Embolism as Primary Cause of Death in 10,650 Necropsies. J. D. Kirshbaum and F. L. Shively Jr., Chicago.—p. 145.
A Method in the Control of Tuberculosis: Case Finding. H. R. Edwards, New York.—p. 148.
*Sulfanilamide in Treatment of Strictures of Rectum Caused by Lymphogranuloma Venereum: Preliminary Report. G. Shropshire, Chicago.—p. 153.
*Streptococci Meningitis: Report of Recovery Following Use of Sulfanilamide Therapy. A. R. Eveloff, Springfield.—p. 162.
Use of Rabies Vaccine in Treatment of Epilepsy. I. S. Schipper, Galesburg.—p. 174.
Complication of Insulin Shock Therapy. H. H. Goldstein, A. P. Bay and J. V. Edlin, Chicago.—p. 175.
Hypotensive Properties of Allium Sativum. E. Podolsky, Brooklyn.—p. 176.
Some Observations on Cancer, Irradiation Reaction and Radiosensitivity. E. N. Kime and D. D. Bowers, Indianapolis.—p. 178.
Studies in Autohemotherapy: Report of Case of Purpura Rheumatica with a New Method of Treatment. L. Saxon, Chicago.—p. 191.

Sulfanilamide and Venereal Lymphogranuloma.—Shropshire gave sulfanilamide orally to nine patients with rectal stricture due to venereal lymphogranuloma. All patients presented a strongly positive reaction to the Frei test and had been under observation for periods varying from one to three years prior to the administration of sulfanilamide. Most of the patients had previous treatment in other institutions. With one exception, all patients received 30 grains (2 Gm.) of sulfanilamide daily in three divided doses for fifteen days. One patient was unable to tolerate sulfanilamide in excess of 20 grains (1.3 Gm.) daily but was given the same total amount over a period of twenty-three days. No other treatment, local or general, was administered. Following this treatment a rest of from seven to ten days was given, after which sulfanilamide was again resumed. Some patients responded more rapidly than others, and the number of periods of treatment varied with the individual response. In five cases the tenesmus, mucous stools, rectal discharge and bleeding completely disappeared under therapy. Two patients with rather extensive involvement of the rectum are still under treatment because of the presence of occasional mucous stools, although the other rectal symptoms have disappeared. The most striking effect of treatment was the rapid improvement in appetite accompanied by an increase in weight and strength. Colostomy had previously been performed in other institutions on two patients. One patient did not suffer from rectal symptoms but complained of a constant, profuse, purulent discharge from the sinus of the left inguinal colostomy, associated with bleeding and frequent evacuations from the transverse colostomy. These symptoms rapidly improved following the administration of sulfanilamide. The other patient was debilitated and complained only of a profuse, rectovaginal, sanguinopurulent discharge, which greatly diminished under treatment and lost its bloody character. These encouraging results prompted the use of sulfanilamide in the treatment of inguinal and vulval types of involvement. To date, only three male patients with inguinal adenitis due to venereal lymphogranuloma have been treated. Sulfanilamide was found to influence this type of involvement favorably but

it failed to cause the adenitis to subside completely. One female patient with chronic ulcers of the vulva, hypertrophic vulvitis and chronic urethritis due to venereal lymphogranuloma has shown definite improvement on sulfanilamide therapy, with prompt response of urinary symptoms and gradual healing of the ulcers. As yet there has been no change in the elephantiasis edema of the vulva.

Johns Hopkins Hospital Bulletin, Baltimore

63: 59-128 (Aug.) 1938

- Clinical and Pathologic Findings in Interauricular Septal Defects: Report of Four Cases. Helen B. Taussig, Baltimore; A. M. Harvey, London, England, and R. H. Follis Jr., Baltimore.—p. 61.
Metabolism of the Isolated Liver. E. Lundsgaard, Copenhagen, Denmark.—p. 90.
Use of Electrocardiogram in the Diagnosis of Adhesive Pericardiomyositis. R. France, Baltimore.—p. 104.
*Influence of Tonsillectomy on the Course of Rheumatic Fever and Rheumatic Heart Disease: Study of 108 Cases. W. B. Allan and J. W. Baylor, Baltimore.—p. 111.

Tonsillectomy and Rheumatic Fever.—Allan and Baylor studied 108 persons with rheumatic fever who had been subjected to tonsillectomy and adenoidectomy. Of the 108 cases, ninety have been followed from ten to twenty-three years and eighteen from one to ten years. The follow-up period of sixteen of the latter group was terminated by the death of the patients. The average age of the eighty-six living patients was 26.4 years in 1935. The eleven patients followed for from one to five years had recrudescences, three single and eight multiple. All the patients in this group died from rheumatic cardiac disease. Fifteen patients were followed for from six to ten years; eight had recrudescences, four single and four multiple. Five of these patients died; two deaths were due to rheumatic cardiac disease, one to tuberculosis, one to erysipelas and one to peritonitis following an appendectomy. Twelve of the thirty-six patients followed for from eleven to fifteen years had recrudescences, three single and nine multiple. There were two deaths in this group, one from rheumatic cardiac disease and one from nephritis. Thirty patients were followed for from sixteen to twenty years and of these twelve had recrudescences, four single and eight multiple. There were three deaths in this group, two from cardiac disease and one from drowning. Of the sixteen patients followed for from twenty-one to twenty-three years four had recrudescences, two single and two multiple. The single death in this group was due to acute rheumatic fever with pancarditis. Since rheumatic cardiac disease developed in only six of the forty-nine rheumatic patients not having cardiac involvement at the time of operation, it is concluded that tonsillectomy and adenoidectomy are to be recommended in the treatment of rheumatic fever. The incidence of persistent infection of the nasopharynx was considerably higher in the patients who had recrudescences than in the entire group. Recrudescences were common in the first five years after operation. Most of the patients who had repeated recrudescences during this period died of rheumatic cardiac disease. Rheumatic cardiac disease occurred more frequently in patients having recrudescences, and deaths from rheumatic cardiac disease occurred only in this group.

Journal of Experimental Medicine, New York

68: 299-456 (Sept.) 1938

- Effect of Sex Hormones on Renal Excretion of Electrolytes. G. W. Thorn and L. L. Engel, Baltimore.—p. 299.
Propagation of Virus of Human Influenza in the Guinea Pig Fetus. O. C. Wolpert, F. W. Gallagher, Leona Rubinstein and N. P. Hudson, Columbus, Ohio.—p. 313.
Altered Cutaneous Conditions in Skin of Tuberculous Guinea Pigs as Demonstrated with Vital Dye. A. L. Joyner and F. R. Sahin, New York.—p. 325.
Studies on Antigenic Structure of Some Mammalian Spermatozoa. W. Henle, Gertrude Henle and L. A. Chambers, Philadelphia.—p. 335.
Effect of Pulse on Formation and Flow of Lymph. R. J. Parsons and P. D. McMaster, New York.—p. 353.
Effect of Pulse on Spread of Substances Through Tissues. P. D. McMaster and R. J. Parsons, New York.—p. 377.
Behavior of Pox Viruses in Respiratory Tract: I. Response of Mice to Nasal Instillation of Vaccinia Virus. J. B. Nelson, Princeton, N. J.—p. 401.
Molecular Weight, Electrochemical and Biologic Properties of Tuberculin Protein and Polysaccharide Molecules. Florence B. Seibert, K. O. Pedersen and A. Tiselius, Philadelphia.—p. 413.
Renal Function as Affected by Experimental Unilateral Kidney Lesions: I. Nephrosis Due to Sodium Tartrate. T. F. Nicholson, R. W. I. Urquhart and D. L. Selby, Toronto.—p. 439.

Journal of Infectious Diseases, Chicago

63: 1-128 (July-Aug.) 1938

- Cause of Anemia in Bartonella Infection of Rats. D. Weinman, Boston.—p. 1.
- Experiments on Metabolism with Diphtheria Bacillus: II. A. Tasman and A. C. Brandwijk, Utrecht, Netherlands.—p. 10.
- Heat Stability and Serologic Activity of Toxic Extracts of Typhoid Bacillus. Elinor Van Dorn Smith, Northampton, Mass.—p. 21.
- Further Observations on Bacteriophage Action in Presence of Blood. W. J. Macneal, Margaret A. McRae and R. A. Colmers, New York.—p. 25.
- Vitamin C and Resistance of the Guinea Pig to Infection with Bacterium Necrophorum. N. B. McCullough, Chicago.—p. 34.
- Regeneration of the Malarial Spleen in the Canary After Infarction and After Burning. W. Bloom and W. H. Taliaferro, Chicago.—p. 54.
- Influence of Ascorbic Acid on Anaphylaxis in Guinea Pigs. S. Raffel and R. R. Madison, Stanford University, Calif.—p. 71.
- Further Studies of Experimental Gonococcal Infection in Mice and Their Protection by Sulfanilamide. A. Cohn and Lenore R. Peizer, New York.—p. 77.
- Observations on Inactivation and Reactivation of Bacteriophage: Studies in Bacterial Metabolism: CX. A. I. Kendall and Charlotte Anne Colwell, Chicago.—p. 81.
- *Possible Mechanism of Lowered Resistance to Pneumonia. W. J. Nungester and R. G. Klepser, Ann Arbor, Mich.—p. 94.
- Excretion in the Urine of Ovalbumin and of Blood Proteins After Intravenous Injection of Crystallized Ovalbumin. Frances A. Briggs, Chicago.—p. 103.
- Improved Medium for Storage of Actinomyces Necrophorus Cultures. E. A. Tunnicliffe, Bozeman, Mont.—p. 113.
- Bactericidal Action of Prostatic Fluid in Dogs. G. P. Youmans, J. Liebling and R. Y. Lyman, Chicago.—p. 117.
- Study of Hemolytic Properties of Streptococci on Various Blood Agars. D. A. Dance and T. J. Murray, New Brunswick, N. J.—p. 122.
- Effect of Simultaneous Inoculation with Various Micro-Organisms on Pathogenesis of St. Louis Encephalitis in Mice. Enid A. Cook, Chicago.—p. 127.

Lowered Resistance to Pneumonia.—Nungester and Klepser discuss a possible mechanism by which exposure to cold, alcoholic intoxication or deep ether anesthesia may lower the resistance of a person to pneumonia. Mucin injected intra-bronchially favored the production of pneumonia in rats sprayed one day later with pneumococci. Certain factors, such as exposure to cold, prolonged deep ether anesthesia or alcoholic intoxication, increased the aspiration of mucous material placed in the nose of rats. Such factors also increased the incidence of pneumonia if pneumococci and mucin were previously inoculated intranasally. Cold or alcoholic intoxication were found to interfere with the closing of the glottis, thereby permitting the aspiration of mucin and pneumococci.

Journal of Lab. and Clinical Medicine, St. Louis

23: 1111-1222 (Aug.) 1938. Partial Index

- Congenital Cystic Lung Disease. D. B. Cole and W. L. Nalls, Richmond, Va.—p. 1111.
- Normal Plasma Phosphatase Values (Jenner-Kay Method). A. S. Mulay and S. Hurwitz, San Francisco.—p. 1117.
- Reaction of Urobilinogen with p-Dimethyl-Aminobenzaldehyde. H. N. Naumann, Brooklyn.—p. 1127.
- Differential Diagnosis of Multiple Myeloma and Hyperparathyroidism by Means of Biopsy. W. W. Sager, R. M. Choisser and G. L. Weller Jr., Washington, D. C.—p. 1132.
- *Clinical Significance of Eosinophilia. R. C. Kirk, Columbus, Ohio.—p. 1137.
- Changes in Colloidal Gold Curve of Normal and Pathologic Spinal Fluids After Ultraviolet Irradiation. J. Warren, New York.—p. 1146.
- Present Status of Staphylococcus Food Poisoning Problem. T. C. Grubb, Baltimore.—p. 1150.
- Effect on Sodium Chloride Crystal Growth of Contamination with Normal and Abnormal Cerebrospinal Fluids. I. Finkelman, Chicago.—p. 1153.
- Sensitization in Convulsive States, with Special Reference to Heterophile Antigen: I. Heterophile Hemolysins. E. W. Lazell, Northport, N. Y.—p. 1160.
- Comparative Study of Selective Mediums for Isolation of Typhoid Bacilli from Stool Specimens. A. A. Hajna and C. A. Perry, Baltimore.—p. 1185.
- Simple Procedure for Diagnostic Culture of Tubercle Bacilli. H. J. Corper, Denver.—p. 1195.
- Method of Collecting Small Blood Specimens, with Special Reference to Microflocculation Tests for Syphilis. J. A. V. Davies, Boston.—p. 1206.
- Use of Swabs Impregnated with Ascitic Fluid in Laboratory Diagnosis of Gonorrhea. R. A. Greene and E. L. Breazeale, Tucson, Ariz.—p. 1211.
- Practical Method of Staining Treponema Pallidum by Means of Low Surface Tension Stain. R. D. Haire, Hobbs, N. M.—p. 1215.

Clinical Significance of Eosinophilia.—Kirk states that if eosinophilia was the result merely of chemotaxis there should be a quantitative relationship between the active agent and the eosinophilia. He has not been able to find this correlation in

the cases of scarlet fever, pemphigus and secondary syphilis. Except for Chillingworth's experiments there is little to be said for the vagal stimulation influence. Holden was able to produce "eosinophils" at will in specimens of urine by altering the pH before centrifuging the white blood cells down and staining them. He suggests this alteration in the pH of the blood, resulting from the induced hyperpnea, as an explanation for Chillingworth's experiments unless these cells were identified by supravital technic, a point which is not mentioned in the original paper. Digitalis intoxications could be equally well explained on a drug sensitivity basis, such as probably occurs in nirvanol medication. Until the true function of the spleen is elucidated, the influence of the spleen on eosinophilia will remain problematic. An allergic basis for eosinophilia seems most likely, the strongest points being the inability to reproduce it by a single injection of foreign protein, and the similar time relationship between the production of eosinophilia and the known production of allergy. There is no postfebrile rise in eosinophils in the cases of typhoid. The reduction is of possible diagnostic significance. The eosinophilia in trichinosis and pemphigus has apparently no prognostic significance.

New England Journal of Medicine, Boston

219: 147-182 (Aug. 4) 1938

- Pressoreceptive Mechanisms for the Regulation of Heart Rate, Vaso-motor Tone, Blood Pressure and Blood Supply. C. Heymans, Ghent, Belgium.—p. 147.
- Experimental Arterial Hypertension. C. Heymans, Ghent, Belgium.—p. 154.
- Role of the Cardio-Aortic and Carotid Sinus Nerves in Reflex Control of Respiratory Center. C. Heymans, Ghent, Belgium.—p. 157.
- Regional Enteritis. C. D. Harvey, J. S. Sprague and G. Clapperton, Boston.—p. 159.
- Prevention and Control of Tuberculosis in Massachusetts. F. T. Lord, Boston.—p. 163.

219: 183-216 (Aug. 11) 1938

- Diet in Prevention of Diabetes Mellitus. D. Adlersberg and S. Siegal, New York.—p. 194.
- Progress in Neurosurgery in 1937. W. Wegner, Boston.—p. 198.

219: 217-250 (Aug. 18) 1938

- Review of 300 General Hospital Patients Admitted to the Boston Psychopathic Hospital During 1937. R. H. Guthrie, Boston.—p. 217.
- Mechanical Obstruction of Small Intestine: Clinical Evidence Against Constipation as a Uniformly Reliable Guide in Diagnosis. J. Fine, Boston.—p. 223.
- *Prostigmine Test in Myasthenia Gravis: Third Report. R. S. Schnab and H. R. Viets, Boston.—p. 226.
- Traumatic Rupture of Thoracic Aorta: Report of Case. J. O. Collins and C. M. D'Alessio, Waterbury, Conn.—p. 229.
- Rack for Holding Hypodermic Needles. A. Solo, Somerville, Mass.—p. 230.
- Heart Disease in Pregnancy. F. B. Carr, Worcester, Mass.—p. 231.

Prostigmine Test in Myasthenia Gravis.—In clinic and office practice the long period of observation formerly used by Schwab and Viets is both impractical and unnecessary. They therefore modified the prostigmine test so that it can be completed in one hour. The best objective symptom for evidence of improvement is determined; for example, degree of ptosis, ability in swallowing, talking, or the muscular strength as measured by ergograph or dynamometer. Three 1 cc. ampules (3 cc.) of prostigmine, to which 0.01 grain of atropine sulfate has been added, is injected intramuscularly. Thereafter at intervals of ten minutes, for an hour, the degree of objective improvement is noted in one column, grading as follows: 0 no improvement, 1 slight improvement, 2 moderate improvement, 3 considerable improvement and 4 complete or marked improvement. In a second column, with the same grading, the patient's subjective opinion of the improvement is scored, giving value to a general feeling of well being. The figures in the two columns are added and the total score is obtained. The maximal score is forty-eight. If the total value is less than eight the test is negative and it is extremely unlikely that the patient has myasthenia gravis. If the total value is from eight to eighteen the test is doubtful and it should be repeated or a therapeutic trial of oral prostigmine should be tried. If the score is more than seventeen (from eighteen to forty-eight) the test is positive. This is presumptive evidence of the diagnosis of myasthenia gravis. In general, the two columns are similar and parallel each other to a striking degree. The test has been used in thirty-five cases of myasthenia gravis, with a score of twenty-five or more. No patient with myasthenia gravis gave

a negative test. In ten the tests were repeated with practically no change in the scores. Owing to the marked change in symptoms of patients with myasthenia gravis after an injection of prostigmine, some observers feel that the need of scoring by making several observations is unnecessary. This is true, perhaps, in three fourths of the myasthenia cases, but in the non-myasthenic group, particularly in chronic cases, suggestion plays a large part and they may score high enough on the subjective symptoms to make the diagnosis of myasthenia possible unless several tests are made. In diseases that simulate myasthenia gravis, negative prostigmine tests were obtained.

Radiology, Syracuse, N. Y.

31: 131-260 (Aug.) 1938

- Hemoptysis and Position of Roentgen Examination in Its Diagnosis: Hickey Lecture of 1938. G. W. Holmes, Boston.—p. 131.
- Congenital Absence of Superficial Volar Arch: Arteriographic Study. P. L. Davis, Philadelphia.—p. 137.
- Six and a Half Years' Experience in Carcinoma Therapy with Extra Hard Roentgen Rays (Fourth Report). E. von Schubert, Berlin, Germany; translation by E. T. Leddy, Rochester, Minn.—p. 142.
- Importance of Indications from Sternal Puncture in Roentgen Therapy. O. Meller, F. Gottlieb and R. Brauner, Bucharest, Rumania; translation by E. T. Leddy, Rochester, Minn.—p. 149.
- Estimation of Dosage from Flat Radium Applicators. M. C. Reinhard and H. L. Goltz, Buffalo.—p. 151.
- Roentgen Therapy in Inflammatory Diseases. H. Wintz, Erlangen, Germany; transcription by A. Payne, Detroit.—p. 156.
- Cranial Radiographic Technique in the Living Rat. E. G. Burr and H. Mortimer, Montreal.—p. 162.
- A Mimicry of Turricophalic Skull in Children Treated on a Bradford Frame. E. P. Pendergrass and P. J. Hodess, Philadelphia.—p. 170.
- True Aneurysm of Right Renal Artery: Case. L. Solis-Cohen and M. Steinbach, Philadelphia.—p. 173.
- Cineradiography by Indirect Method. R. Reynolds, London, England.—p. 177.
- Direct Visualization of Axillary and Subclavian Veins. J. R. Veal, Washington, D. C.—p. 183.
- Pelviccephalometry. R. P. Ball, New York.—p. 188.
- Nomogram for Roentgenographic Mensuration. H. J. Holmquest, Chicago.—p. 198.
- *Stray Radiation Survey of Twenty High Voltage Roentgen Installations. C. B. Braestrup, New York.—p. 206.
- Roentgen Diagnosis of Fracture of Skull: Review of 1,135 Cases So Diagnosed. R. A. Rendich and B. Ehrenpreis, Brooklyn.—p. 214.
- *Roentgen Treatment of Plantar Warts. W. C. Popp and J. W. Olds, Rochester, Minn.—p. 218.

Stray Radiation.—Braestrup made measurements to establish the relationship between the stray radiation and the type as well as the amount of protection provided in different high voltage x-ray installations using similar operating conditions. A description of the instruments used is given. Under normal operating conditions all the investigated enclosed tube holders provide sufficient protection to the patient. The term ray proof, which at present generally is applied to tube heads, is somewhat ambiguous. None of the measured tube heads permit routine manipulation with safety while the x-ray tube is excited although the shutter is closed. More effective shielding of the direct radiation is essential in cases in which it is desired to operate the tube continuously and have the shutter control the timing of the treatments. It is suggested, therefore, that the term ray proof be limited to tube enclosures from which the stray radiation does not exceed 0.036 roentgen per hour at 1 meter focal distance in any direction and with the tube operating at its normal rating. Tube enclosures with less shielding but still providing ample protection to the patient could then be described as x-ray protective or radiopaque if the stray radiation does not exceed 1 roentgen hour under the foregoing conditions. Measurement of stray radiation from the different installations indicates that a high factor of safety can be obtained at a much reduced cost if greater consideration is given to the arrangement of the protective materials. Several cases of insufficient protection were corrected as a result of this survey.

Roentgen Treatment of Plantar Warts.—Popp and Olds determined the effect of roentgen treatment of ninety-one patients with plantar warts. These patients came from a distance and the study was made with the thought in mind that it might serve as a method of determining the effect of the initial treatment, which was expected to cure the lesion and might suggest a technic that would reduce to a minimum the number of refractory cases. The lesion was single in fifty-four cases and multiple in thirty-seven; the frequency of occurrence was equal in the two feet. In eleven instances the warts occurred

on both feet. Fifty-eight patients obtained complete cure, whereas eighteen received no benefit. Cure, following subsequent treatment elsewhere, was reported by six patients; six others obtained merely relief of pain, and only partial or temporary relief was obtained in three instances. In forty of the fifty-eight cured patients the lesion or lesions disappeared after one treatment. Eleven patients required two treatments, five required three and two were cured only after four treatments. The average interval between the beginning of treatment and the disappearance of the lesions was six weeks. In thirty-two of the cured cases, removal of the wart was accomplished with a total of two and one-half skin erythema doses (one such dose equals 400 roentgens in air) of unfiltered radiation generated at 80 kilovolts, five patients received three skin erythema doses and seven only two doses, seven others received from two-thirds to three doses in one to three treatments over a period of time, and seven were given from one half to two doses of filtered radiation with 2 mm. of aluminum filtration at 100 kilovolts in addition to from one to two doses of unfiltered radiation. Of the eighteen patients who did not benefit from the treatment, eleven patients received two and one-half, one three, four from two-thirds to three skin erythema doses and two received both filtered and unfiltered radiation. Recently the authors have employed a technic using 100 kilovolts, 0.5 mm. of aluminum filtration at a distance of 40 cm., applying three doses. Early observations indicate that this technic may offer better curative results than other technics.

Review of Gastroenterology, New York

5: 226-305 (Sept.) 1938

- Sprue and Pernicious Anemia. A. Castellani, New Orleans.—p. 226.
- Bacteriology of Intestinal Tract in Certain Diseases: II. Possible Inhibition of Colon Bacilli by Pathogenic Streptococci and Staphylococci. G. H. Chapman and C. W. Lieb, New York.—p. 234.
- Food Allergy of Digestive System. J. S. Smul, New York.—p. 241.
- Some Hints in Office Proctology. J. L. Mathesheimer, Jersey City, N. J.—p. 254.
- Unusual Kidney Stone. D. A. Meiselas, Brooklyn.—p. 258.

Southwestern Medicine, El Paso, Texas

22: 301-344 (Aug.) 1938

- Psychiatric Complications Frequently Encountered in General Practice. F. G. Ebaugh, Denver.—p. 301.
- Evaluation of Factors in Bone Union. E. C. Houle, Nogales, Ariz.—p. 307.
- *Comparison of the Eagle, Ide, Kahn, Kline and Laughlen Tests for Syphilis. E. L. Breazeale, R. A. Greene and H. B. Harding, Tucson, Ariz.—p. 311.
- Surgical Treatment of Pulmonary Tuberculosis. F. P. Miller, El Paso, Texas.—p. 313.
- Dental Fluorosis in Lea County, New Mexico. D. C. Badger, Hobbs, N. M.—p. 317.
- Jaundice: A Symptom of Significance. J. J. Gorman, El Paso, Texas.—p. 318.
- Treatment of Toxemia of Pregnancy. P. T. Brown, Phoenix, Ariz.—p. 322.

Comparison of Tests for Syphilis.—Breazeale and his associates compared the reliability of the Eagle, Ide, Kahn, Kline and Laughlen tests for syphilis: The agreement between the tests varied from 98.5 to 99.5 per cent. With 1,000 serums, all tests agreed with the exception of seventeen (98.3 per cent). In four instances, one test gave a doubtful reaction (+) when the other tests were negative; in the remaining cases at least two or more of the tests employed agreed. In the exceptions the variation was in weakly positive serums. In no instance was the Kahn reaction strong enough to be considered diagnostic (2 plus). Among the positive serums there was no instance in which there was any lack of agreement in the results obtained by the various technics. In 107 serums the results which the authors obtained agreed with the Wassermann tests obtained in three other laboratories in all but six cases. These were serums which had given negative or weakly positive Wassermann reactions. From the results which they obtained they feel that, when proper attention is given to the performance of the test, the different methods are equally reliable. Judging from their experience they believe that lack of agreement is probable only in serums which gave doubtful (+) or weakly positive reactions. The percentage of these is approximately the same for all tests. The choice of a test should be governed by the equipment available.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Journal of Radiology, London

11: 505-568 (Aug.) 1938

- Paget's Disease of Bone: Its Frequency, Diagnosis and Complications. J. F. Brailsford.—p. 507.
Effect of Gamma Radiation on Cells in Vivo: Single Exposures of Normal Tadpole at Room Temperature. F. G. Spear and A. Glücksmann.—p. 533.
Theory of Action of Radiations on Biologic Materials Capable of Recovery: Part II. Delay in Cellular Division. D. E. Lea.—p. 554.

British Journal of Surgery, Bristol

26: 1-216 (July) 1938

- Trephiners of Blanche Bay, New Britain, Their Instruments and Methods. I. Brodsky.—p. 1.
Intrathoracic Reconstruction of the Lower Esophagus: Note on Unsuccessful Case. W. H. Ogilvie.—p. 10.
Pathology and Treatment of Recurrent Dislocation of the Shoulder Joint. A. S. B. Bankart.—p. 23.
Primary Actinomycosis of the Breast. P. N. Ray and B. P. Tribedi.—p. 30.
Gastroscopic Appearances in Health and Disease. J. H. Hughes.—p. 35.
Pleuro-Esophageal Fistula in Empyema. H. Blauvelt.—p. 46.
Riedel's Thyroiditis and Its Treatment by Radium. J. M. Renton, A. A. Charteris and J. F. Heggie.—p. 54.
Acute Infective Osteomyelitis of the Spine. P. Turner.—p. 71.
*Intra-Arterial Glycerin Treatment of Elephantiasis. C. Bowesman.—p. 86.
Plasmodioma of Innominate Bone. J. C. Leedham-Green, J. F. Bromley and J. Raban.—p. 90.
Nerve to Extensor Carpi Radialis Brevis. C. R. Salisbury.—p. 95.
Urinary Calculi Developing in Recumbent Patients. L. N. Pyrah and F. S. Fowweather.—p. 98.
*Periodicity in Cancer and Other Neoplastic Diseases (450 Cases). J. H. D. Webster.—p. 113.
Anterior Basal Meningiomas. W. R. Henderson.—p. 124.
Tumor of Lung. A. T. Edwards.—p. 166.
Esophageal Polypus Accompanied by Tumor of an Accessory Thyroid Gland: Case. E. C. Chitty.—p. 193.

Glycerin Treatment of Elephantiasis.—Bowesman gave intra-arterial injections of from 2 to 3 cc. of sterile 10 per cent glycerin at intervals of one week to sixteen patients with elephantiasis and intravenous injections to four patients. The treatment alleviated to some extent the elephantiasis of the leg due to filaria. The intra-arterial injections are made into the femoral artery. Intravenous injections produce a less definite effect. The dull aching discomfort is lessened. Patients seen five months after cessation of the treatment showed limbs which either had the same size as at the end of treatment or remained smaller than before the commencement of treatment. Patients affected for two years or less appeared to improve until the measurements of the limb became equal. Patients suffering from the disease between two and four years were relieved of the chronic dull aching discomfort and showed a diminution of the measurements of the limb. These measurements never became normal, i. e. equal to the unaffected limb. All patients were improved to some extent, and there were no complications.

Periodicity in Neoplastic Diseases.—Webster traced the recurrence of 450 cases of neoplasm. The series includes carcinoma, sarcoma, recurrent papillomas, leukemia and lymphadenoma (with possibly Mikulicz's disease and other benign neoplasms). Periodicity has been clearly present in 96 per cent of the cases analyzed: usually it has been seen in a period of eight lunar months (thirty-three weeks); often in four lunar months (sixteen and a half weeks). The periodicity has been recognized most easily in superficial recurrences or in those readily accessible to clinical examination or to demonstration by x-rays. Neither surgical treatment nor irradiation has appeared to have an influence on periodicity. This has been shown by patients for whom a peak of rapid growth had been determined before the treatment began: recurrences followed at periods or half periods irrespective of the treatment. The alternatives appear to be cure or periodicity. For a high degree of statistical accuracy a series of patients with recurrent tendency should be examined at weekly intervals before and during probable recurrent maximums. The most conclusive proof of periodicity would appear to be success in prediction of recurrences, and already several successful predictions have been made. Full periods have been seen more than twice as often

as half periods in cases of carcinoma and leukemia. In eighteen patients with multiple primaries the signs of onset of the primaries (and any recurrences) have all fallen within one periodic scheme, as though each patient had had one disease with differing site manifestations. Neoplastic periodicity seems to bring forward circumstantial evidence in favor of the virus theory of cancer, as discussed by Gye and referred to by Webster. A virus origin is probable for human leukemia and lymphadenoma (proved for some skin papillomas, fowl leukemia and fowl sarcoma) and no other cause for the periodicity but a virus presents itself. Analysis of the dates of recurrence has shown that in breast cancer, sarcoma, leukemia and Hodgkin's disease almost half as many again recurrences have been seen in the first four months of the year as in each of the two other four month groups. This finding confirms the observations of Peacock and of Fraenkel on seasonal periodicity in animal tumors. The half periods may indicate a double infection, as in a double tertian malaria infection. (Half periods have been seen most commonly in sarcoma and Hodgkin's disease.) The signs in several patients have suggested a double infection. On a virus theory, either a chemical change or a stimulus occurs, or a vital reproduction occurs, at the half period instead of at the full term or its multiple, owing either to inherent seasonal or other accentuation of growth or to the patient's loss of resistance. Important practical applications of neoplastic periodicity are suggested in the fields of prevention, diagnosis, prognosis and treatment.

British Medical Journal, London

2: 273-330 (Aug. 6) 1938

- Physiologic Approach to Fitness. E. P. Cathcart.—p. 273.
Skiagraphy of the Chest. G. Jessel.—p. 276.
*Clostridium Welchii Infection Following Abortion: Three Cases. R. Y. Dawbarn and B. Williams.—p. 279.
Certain Phases in Life History of Polymorph Leukocyte: Influence of Cell Activity on Number and Arrangement of Nuclear Lobes. C. J. Bond.—p. 281.
Chemotherapy in Gonorrhea: Preliminary Report on Use of 2-(p-Amino-benzene-sulfonamido) Pyridine. F. J. T. Bowie.—p. 283.
X-Ray Pelvimetry: Simple Method for Measuring Pelvic Brim. A. Orley.—p. 284.

Clostridium Welchii Infection Following Abortion.—Dawbarn and Williams cite three fatal cases of infection with *Clostridium welchii* following abortion. In two of these the infection was a fulminating one in which the main feature was the occurrence of hemolysis, and a correct diagnosis was not made before death. The third case was one of a rapidly fatal infection of the uterus. In the two cases of septicemia the onset was so sudden and the manifestations were so dramatic that chemical poisoning was suspected. These suspicions were strengthened by the fact that both patients had been taking large doses of pills, presumably with the object of procuring abortion. The third patient also had a fulminating infection, although the clinical picture was different and the diagnosis was made soon after admission to the hospital. After death *Clostridium welchii* was found in various tissues in cultures, smear and films. In none of the three patients was the mode of infection determined. In every instance the pregnancy was an unwanted one, and all patients admitted having taken drugs with the object of procuring abortion, so that it seems probable that instrumental intervention had also been attempted.

Edinburgh Medical Journal

45: 529-604 (Aug.) 1938

- Primary Toxic Goiter. J. Eason.—p. 529.
XXVI. Treatment of Minor Foot Disabilities. T. M. Millar.—p. 540.
*Neuropsychiatric Aspects of Bromide Intoxication. H. Tod and J. Stalker.—p. 561.
Modern Developments in the Organization of Treatment of Fractures. W. A. Cochrane.—p. 576.
Can We "Breed Out" Cancer in the Human Race? Madge Thurlow Macklin.—p. 587.

Neuropsychiatric Aspects of Bromide Intoxication.—Tod and Stalker aver that not only do physicians abuse bromides but that bromides are a common constituent of the "patent medicines" at which the neurotic, the sleepless, the depressed and many other unstable people snatch so readily. Many patients on admission to the Royal Edinburgh Hospital for mental disorders are in a toxic physical state and may show mental symptoms of a toxic kind in addition to those of the original disease; the

blood contains bromide and the toxic symptoms disappear when the drug is withheld. During the last four years at least ten patients have been admitted suffering from a frank bromide psychosis; two of these died from bromide intoxication. The clinical symptoms and signs are numerous and may appear in any order, in any combination and in any intensity. It not infrequently happens that when a patient is receiving bromide her anxiety, depression, agitation, excitement and the like become worse; occasionally the drug produces depression. The body is unable to distinguish between bromides and chlorides; consequently ingested bromide is found in the body wherever chloride is found. Consequently a diet poor in salt favors the retention of bromide in the organism. Prescribing bromide without knowing the chloride intake or the bromide saturation is the same as letting the patient take as much or as little bromide as he pleases. Any condition which might in any way impair the halogen excretion by the kidney predisposes to intoxication, e. g. all forms of dehydration, nephritis, arteriosclerosis, hypertension and pneumonia in which the halogen excretion almost completely stops. Persons who are weak, infirm or bedridden or who take little exercise are also predisposed. Any impairment of the function of the kidney predisposes to intoxication. Bromide intoxication may in itself impair the function of the kidney and so set up a vicious circle. The clinical features of bromide intoxication are essentially those of an organic reaction type (acute or chronic, mild or severe); that is, impairment of comprehension, interference with the elaboration of impressions, defects in orientation and retention, difficulty in activation of memories, marked fluctuation in the level of attention and emotional instability. There may be any gradation from a mild or chronic process to an acute delirium and the typical neurologic signs may also be present in any degree. Bromide intoxication may simulate any form of organic reaction; but whether the mental disorder is organic or functional a careful history in which the symptoms that led to the taking of bromide are differentiated from those which followed its use, the blood bromide estimation, the effect of withdrawing the drug and in some cases the neurologic signs should assist in making the diagnosis. The rate at which the symptoms clear up depends on the degree of intoxication, the integrity of the kidneys and the efficacy of treatment. The aims of treatment are to displace the bromide from the body and to sustain the patient's strength during the period of intoxication. The administration of sodium chloride in large amounts causes a rise in the amount of halogen and consequently of bromide excreted. Salt is best given in capsules in doses of 4 Gm. three times a day. The intestine and bladder should be attended to; constipation is frequent and retention of urine occasionally occurs. A patient in delirium requires the most careful nursing, and when possible he should be in the quiet of a single room with a special nurse. Most sedatives are dangerous in such cases as they increase the toxemia, but, if the patient is sleepless, paraldehyde should be given at night.

Indian Medical Gazette, Calcutta

73: 385-448 (July) 1938

- Anahemin in Tropical Macrocytic Anemia. L. E. Napier, C. R. Das Gupta, R. N. Chaudhuri, G. N. Sen, M. N. Rai Chaudhuri, P. C. Sen Gupta and D. N. Majumder.—p. 385.
Protamine Zinc Insulin. J. P. Bose.—p. 390.
Note on Therapeutic Efficiency of Solu-septasine in Simian Malaria (Plasmodium Knowlesi). R. N. Chopra and B. M. Das Gupta.—p. 395.
Some Observations Concerning Recent Typhoid Epidemic in Calcutta. H. E. Murray, with Note on Typhoid Myocarditis. G. Kelly.—p. 396.
Malaria in Relation to Coastal Lagoons of Bengal and Orissa. C. Strickland.—p. 399.
Color Perception and Color Blindness Tests. C. E. R. Norman.—p. 402.
Vibrio Cholerae from Material Obtained by Liver Puncture During Life. C. L. Pasricha, A. J. H. DeMonte and B. C. Chatterjee.—p. 405.
Cholera Epidemics in Burma and Type of Vibrio Associated with Them. G. C. Maitra, P. N. Sen Gupta and U. Thant.—p. 406.
*Observations on Mottled Condition of Human Teeth Endemic in a Certain Locality of Nagercoil in Travancore, South India. S. C. Pillai.—p. 408.
A Rat-Flea Survey of Mattanchery (Cochin, 1937). P. Mohamed Ali.—p. 409.
Experiments on the Stability of Seminal Stains from a Medicolegal Standpoint. S. N. Chakravarti and S. N. Roy.—p. 412.

Mottled Teeth Endemic in Travancore.—Pillai observed that a section of the people (about 100 families) residing at one end of the town of Nagercoil in South Travancore has mottled teeth. The enamel of the teeth of these people, particularly in

the case of the adults and the older members of the community, would appear to have been subjected to a sort of corrosion followed by pigmentation. In addition to the pigmented condition and the consequent disfigured appearance, the mottled teeth have also been found to be defective in structure and strength. The analysis of the drinking water supply of the affected persons shows the presence of from 0.4 to 0.5 part per hundred thousand of fluorine, whereas the water supplies for the other sections of people contain practically no fluorides. In other respects the composition of the incriminated water is similar to that from adjoining areas.

International Journal of Psycho-Analysis, London

19: 291-375 (July) 1938

- Moses an Egyptian. S. Freud.—p. 291.
Development of Awareness of Transference in a Markedly Detached Personality. Clara Thompson.—p. 299.
Mode of Operation of Psychoanalytic Therapy. Melitta Schmeideberg.—p. 310.
Pseudo-Identification. L. Eidelberg.—p. 321.
Contribution to the Pathopsychology of Phenomena Associated with Falling Asleep. O. Isakower.—p. 331.

Journal of Hygiene, London

38: 395-520 (July) 1938

- Classification of Coliform Bacteria. J. F. Malcolm.—p. 395.
Effect of Diet on Epidemics of Mouse Typhoid. Marion Watson, Joyce Wilson and W. W. C. Topley.—p. 424.
*Investigation of Effects of Certain Substitutes for Morphine and Heroin on Passage of Food Along Alimentary Tract of Human Subject. G. N. Myers and S. W. Davidson.—p. 432.
Distribution of Coliform Organisms in Milk and Accuracy of Presumptive Coliform Test. H. Barkworth and J. O. Irwin.—p. 446.
Pleuropneumonia-like Organisms of Diverse Provenance: Some Results of Enquiry into Methods of Differentiation. Emmy Klieneberger.—p. 458.
Antigenic Structure of Mannitol-Fermenting Group of Dysentery Bacilli. J. S. K. Boyd.—p. 477.
Is General Paresis Dependent on Previous Treatment with Mercury? P. Heiberg.—p. 500.
Isolation of Bacterium Typhosum by Means of Bismuth Sulphite Medium in Water and Milk-Borne Epidemics. W. J. Wilson.—p. 507.

Substitutes for Morphine.—Myers and Davidson studied the effect of dihydromorphinone hydrochloride (dilaudid), dihydrocodeinone (dicodid), hydrochloride of dihydroxycodeinone (eukodol), diacetylmorphine and morphine on the human alimentary tract in young healthy adult male medical students. Barium sulfate meal and x-ray methods were made use of for the observations. The effects of dilaudid closely resemble those of morphine. Dilaudid produces a condition of increased tone in the pyloric and ileocolic sphincters resulting in delayed emptying of the contents of the stomach into the duodenum and a delayed passage of the intestinal contents into the cecum. Dicodid has a much weaker action on the pyloric and ileocolic sphincters than either morphine, diacetylmorphine, dilaudid or eupodol. It causes only a negligible delay in the passage of food up to the time of three hours, it being normal at six hours owing to a hastening of the motility rate. Eukodol has an action resembling that of morphine. All these drugs possess well marked analgesic properties. No gross rectal symptoms were observed in any of the subjects under observation.

J. Royal Inst. Public Health and Hygiene, London

1: 629-694 (Aug.) 1938

- *Muscle Action in Relation to Repair of Joint Tissues. M. Smart.—p. 639.
Women and Children and Public Health. Lady Roney.—p. 651.
*Conquest of an Occupational Disease: Phosphorus Poisoning in Lucifer Match Making. T. Oliver.—p. 660.
Influence of Noise on Health. J. Purves-Stewart.—p. 667.
Diet in Pregnancy. Louise McIlroy.—p. 672.
Emotional Adjustment in the Health of the Adolescent and Its Bearing on Physical Fitness. D. Shields.—p. 676.
Chronic Miliary Tuberculosis. C. Hoyle.—p. 682.

Muscle Action in Repair of Joint Tissues.—Smart declares that in order to maintain a tissue in a healthy state the regular normal fulfilment of the function of the arterial, venous and lymphatic circulations is essential. He shows the great part played by muscular contraction and relaxation in promoting these circulations and in aiding the removal of fluids infiltrated into the tissues. Movement—that is muscular action—therefore plays a special part in the efficiency of the circulatory system generally, and conversely when muscles are

hypotonic and wasted, the physical and chemical phenomena coincident with their normal activity, which is so essential to their efficiency and sensation of well being, are seriously interfered with, and this has a detrimental effect on the nutrition not only of the muscles but of all the neighboring tissues as well. It is possible by the application of a properly designed electrical unit to utilize muscular activity in the treatment of inflamed and painful joints. The correct application of the right type of electric current reproduces painless alternate contractions and relaxations of the muscles and, provided the rate and degree of the contractions and the relaxations are under perfect control, there is no more potent means of stimulating rapid and complete absorption of fluids from the tissues. Controlled stimulation of muscles to produce alternate contractions and relaxations restores the tone to the muscles, prevents intermuscular and intramuscular adhesions by keeping the tendons and other parts moving, and increases the blood and lymph supply and the onward movement of tissue fluids, thus stimulating the rate of repair by encouraging the rapid absorption of waste products. The method is used solely to encourage the restoration of normal function by artificial stimulation, with all the attendant beneficial changes resulting from muscular action, only during the period that normal muscular function is lost or diminished. Muscular stimulation rapidly restores the tone and redevelops wasted muscular atonicity, which, if reached, no amount of voluntary exercise, even when combined with skilled and prolonged massage, will produce complete redevelopment, whereas the response to artificial electrical stimulation is striking and, provided the path of the nerve is intact, ends in certain and rapid recovery and even overdevelopment if pushed too far.

Phosphorus Poisoning in Match Making.—Oliver states that, since Sevéne and Cahen of France recommended the substitution of phosphorus sesquisulfide for white phosphorus, a safe and equally useful substitute had been found for the manufacture of the "strike anywhere" match. Never since in Great Britain has there been recorded a case of suicidal or accidental phosphorus poisoning or any new cases of phosphorus necrosis or illness among the workers. At an international convention in Berne in 1906 many of the civilized nations supported this line of action and a few years ago China and Japan also joined the convention, so that under present conditions it is hardly likely that one shall ever again hear of phosphorus poisoning, and certainly never of industrial phosphorus necrosis.

Journal of Tropical Medicine and Hygiene, London

41: 245-260 (Aug. 1) 1938

- Failure to Transmit an Infection of *Plasmodium Cynomolgi* to Man by Blood Inoculation and by Mosquito Bites. J. A. Sinton, E. L. Hutton and P. G. Shute.—p. 245.
Cultivation and Pathogenicity of *Diendamoeba Fragilis*: Case Report. M. Mollari and J. V. Anzulovic.—p. 246.
Trypanosomiasis Gambiense: Some Observations in Uganda and Their Bearing on Prophylaxis. A. A. F. Brown.—p. 247.

Lancet, London

2: 295-350 (Aug. 6) 1938

- Approach to Gastric Surgery. W. H. Ogilvie.—p. 295.
Intermittent Fever of Three and a Half Years' Duration. J. W. Scott and A. Kirshner.—p. 299.
*Faulty Detoxication in Schizophrenia: Abnormal Excretion of Hippuric Acid After Administration of Benzoate. J. H. Quastel and W. T. Wales.—p. 301.
Purpura Haemorrhagica (Werlhof) After Taking Sedormid. T. Joekes.—p. 305.
Hyperplasia of the Male Breast Accompanying Malignant Disease of Testis Treated by X-Rays. C. W. B. Woodham.—p. 307.
Treatment of Marasmus by Injection of an Extract of Adrenal Cortex. W. A. Hislop.—p. 308.

Faulty Detoxication in Schizophrenia.—Quastel and Wales propose to demonstrate that catatonic patients as a class show a definite disability to detoxicate benzoic acid at a normal rate and imply that in this subgroup of schizophrenic patients there is present an abnormality which is concomitant with the development of the psychosis and may be partly responsible for it. Sixty-seven patients were chosen who on thorough examination showed no evidence of hepatic or renal disorder. Of the sixty-seven patients, forty-five were schizophrenic and eighteen of these were classified as catatonic. Twenty-three of twenty-seven noncatatonic patients in the schizophrenic group gave

hippuric acid excretions of the normal value and normal range of variation. Of the eighteen catatonic patients, all without exception gave values lower than the average normal. A number of these patients were examined on more than one occasion at intervals of several weeks. The average value of benzoic acid excreted in the schizophrenic noncatatonic group was 3.4 Gm. and the average deviation from the mean was ± 0.4 Gm. The average value of benzoic acid excreted in the catatonic group was 2.2 Gm. and the average deviation from the mean was ± 0.5 Gm. Among the twenty-two nonschizophrenic patients (of whom twelve fall into the manic-depressive group) several gave diminished outputs of benzoic acid. The results suggest that a metabolic disturbance is present, probably in the liver. The phenomenon appears to present a metabolic abnormality existing in catatonic patients. None of the catatonic patients studied had had chemotherapy for several weeks, so that the results cannot be complicated by this factor. The results are unlikely to be due to a deficiency of amino acid. The fact that all the catatonic patients showed a diminished ability to excrete hippuric acid after benzoate administration makes it unlikely that the phenomenon is purely fortuitous. The phenomenon may also find an explanation in delayed absorption of benzoate or of aminoacetic acid from the intestine. Experiments to determine this are now in progress. The long duration of illness of the catatonic patients may be related in some manner to the impairment of benzoate detoxication.

Medical Journal of Australia, Sydney

2: 109-144 (July 23) 1938

- Radiology: The Past and the Future. H. M. Hewlett.—p. 109.
The Radiologic Examination of the Heart. L. E. Rothstadt.—p. 116.
Cystic Tumors of Third Ventricle. L. C. E. Lindon.—p. 122.
Ether Anesthesia and Analgesia in Midwifery. T. H. Small.—p. 124.
Gettler's Test in Cases of Drowning. A. Palmer.—p. 129.
*Preliminary Observations on Virus Responsible for Victorian and Tasmanian Epidemics of Poliomyelitis, 1937. F. M. Burnet and E. V. Keogh.—p. 130.
2: 145-184 (July 30) 1938
Mental Hygiene of the Preschool Child. J. F. Williams.—p. 145.
Nutrition of the Preschool Child. Vera Scantlebury.—p. 148.
The Training of the Preschool Child. Christine Heinig.—p. 155.
Hematuria. K. Kirkland.—p. 159.
Goiter and Thyreotoxicosis. A. E. Lee.—p. 162.

Poliomyelitis in Victoria and Tasmania.—Burnet and Keogh isolated a typical poliomyelitis virus from spinal cords of several patients who had died during the 1937 Victorian and Tasmanian epidemics of poliomyelitis. All the monkeys that were inoculated from the cords had typical symptoms, with some variability in the incubation period. The shorter the incubation period, the more severe were the symptoms. On the whole, the virus appears to be more readily transferred to the monkey than strains obtained in nonepidemic periods. The variability in intensity of symptoms was also evident in sub-inoculations. Monkeys recovered after infection with the virus are still partially susceptible to infection by the Rockefeller Institute MV strain.

Practitioner, London

141: 117-236 (Aug.) 1938

- Basis of Physical Medicine. L. Hill.—p. 117.
Prescription of Physical Treatment in General Practice. J. Mennell.—p. 124.
Hydrotherapy and Spa Treatment. G. Holmes.—p. 133.
Electrotherapy in General Practice. E. P. Cumberbatch.—p. 145.
Uses and Abuses of Ultraviolet Radiation. A. Eidinow.—p. 154.
Infra-Red Irradiation. W. Beaumont.—p. 161.
Massage in General Practice. E. B. Clayton.—p. 169.
Affections of the Nails. W. J. O'Donovan.—p. 177.
Vertigo, Its Causes, Diagnosis and Treatment. C. P. Symonds.—p. 186.
Treatment of Bacillary Dysentery with Bacteriophage. J. E. Murray.—p. 199.
Diet in Health and Disease: XIV. Diet in the Tropics and Tropical Diseases. W. E. Cooke.—p. 202.

Chinese Medical Journal, Peiping

54: 101-200 (Aug.) 1938

- Roasted Soybean in Infant Feeding. R. A. Guy and K. S. Yeh.—p. 101.
Retroposition of the Uterus. Y. K. K'o.—p. 111.
Disruption of Abdominal Wounds. H. E. Campbell.—p. 131.
Human Infection of *Hymenolepis Nana* in North China: Analysis of 171 Cases. L. S. Wang.—p. 141.

Bruxelles-Médical, Brussels

18: 1334-1360 (Aug. 14) 1938

Sedimentation of Erythrocytes as Differential Diagnostic Factor in Acute Adnexitis, Appendicitis and Extra-Uterine Pregnancy. J. A. Schockaert, J.-P. Rosman and H. Nolens.—p. 1334.

*Histamine Therapy in Rheumatic Pains. D. Vincart-Van Geem.—p. 1345.

Histamine Therapy in Rheumatic Pains.—Vincart-Van Geem, after reviewing the previous history of histamine therapy in the form of ionization or dielectrolysis, discusses the chemistry and the mode of action of histamine. Then he points out that investigations by Deutsch revealed that muscles normally require a certain quantity of histamine, which they liberate spontaneously in the course of movement and exercise. If the muscles are more or less immobilized by a pathologic condition like that of rheumatism, the resulting deficiency in histamine intensifies the pathologic state and produces contracture with all its consequences: pain, articular ankylosis, muscular contracture, capillary disturbances and so on. For this reason it was decided to introduce histamine. Discussing its mode of administration, the author says that ionization and intradermic injection are the methods of choice. Ionization with histamine was first employed by Ebbecke in 1922 and Deutsch adapted this method. The author himself slightly changed the technic employed by Deutsch. He uses several thicknesses of gauze, which are saturated with a solution of histamine dihydrochloride (10 mg. per liter of distilled water) and which are covered with a metallic foil. This electrode is applied to the skin and it is connected with the positive pole of a source of galvanic current. The other electrode, which is saturated with water, is connected with the negative pole and during the treatment it is held in the patient's hand. The intensity of the current varies between 3 and 10 milliamperes; the time of application is inversely proportional to the current strength. The author found that three minutes with 5 milliamperes was the most convenient form of application for the majority of patients. The intradermic injection of histamine employs ampules of 1 cc., containing 0.5 mg. of histamine dihydrochloride in an isotonic solution, the pH of which is around 7. One or two drops of the solution is deposited into the skin at distances of 1 or 2 cm. From fifty to seventy-five can be made with one ampule. In one group of patients the ionization treatment and the intradermic application were given on alternate days, but the ionization treatment was preferred by most of the patients. Regarding the indications for the histamine therapy, the author says that he considers it advisable in all acute and chronic myalgias, in arthralgias due to acute and chronic periarthritis, in the sequels of infectious rheumatism, in traumatism such as fractures and sprains, in essential or secondary neuralgias, in rheumatism and in cellulitis. However, the treatment is contraindicated during the evolutive period of acute infectious rheumatism.

Journal de Chirurgie, Paris

52: 145-288 (Aug.) 1938

Treatment of Grave Paralytic Talipes Calcaneus. J. Leveuf and P. Bertrand.—p. 145.

*Indications for and Technic of Retroglenoid Abutments in Posterior Dislocations of Shoulder. Fèvre and J. Mialaret.—p. 156.

Surgical Technic of Treatment of Posterior Marginal Fractures of Tibia

Under Roentgenologic Control. R. M. D'Aubigné.—p. 168.

Pegging in Diaphysal Fractures. H. Lafitte.—p. 177.

Retroglenoid Abutments in Posterior Dislocations.—Fèvre and Mialaret stress the advantages of applying in relapsing posterior dislocations of the shoulder the excellent procedure of abutment, which is so frequently employed in the anterior dislocations. They say that this method is not entirely new, it having been employed with good success by Rocher and others. But although Rocher had given a detailed description of the technic, the procedure seemingly has not entered current practice. The posterior dislocations justifying this intervention are rare; in adults only 3 per cent of the relapsing dislocations are retroglenoid. In children, however, these dislocations seem to be more frequent, but the abutment has as yet not received the attention it deserves in the treatment of congenital dislocations of the shoulder. The authors report their own experiences with this treatment in a child aged 11.

The functional results obtained in this case were perfect. Following a detailed description of this case the authors discuss the indications for this intervention and then give a detailed description of the technic. They first describe the withdrawal of the grafts from the tibia and, in discussing the intervention on the shoulder, they say that in simple cases the retroglenoid abutment can be executed by a subdeltoid posterior incision. In the difficult cases (difficulty of reduction, of maintenance of head of humerus) the intervention is more extensive; the classic method of Duplay-Kocher is used or it is modified and simplified for children.

Presse Médicale, Paris

46: 1225-1232 (Aug. 10) 1938

*Painful Syndromes of Extensive Invasion of Skeleton in Patients with Cancer of Breast. J. Ducuing.—p. 1225.

Skeletal Syndromes in Cancer of Breast.—According to Ducuing, cancer of the breast gives rise to osseous metastases more frequently than was formerly believed. These metastases may be circumscribed and isolated or diffuse and extensive. Although a secondary isolated nucleus can be extremely painful, the author gives his attention chiefly to the study of the pain in the course of the extensive invasion of the skeleton. The cancerous invasion of the bones is not always painful; it may evolve insidiously to the cachectic state or until it becomes manifest either by a spontaneous fracture or by an osseous thickening. The conditions described here are essentially the painful manifestations of isolated osseous involvement; the patient suffers "in the bone," but these pains precede quite frequently the signs of medullary radicular and truncal invasions or compression, which constitute the syndromes described by neurologists. But the lesions which cause the osseous pains do not always terminate in those that provoke the nervous syndromes; in some cases they remain localized in the skeleton. After citing the various mechanisms of osseous invasion (by way of the blood and the lymphatics), the author says that anatomoroentgenologic studies reveal that there are three principal types of extensive invasion of the bones by mammary cancer. In his opinion, every extensive invasion into the osseous system begins with vertebral involvement; then the lesions spread to the shoulder girdle and then to the pelvic girdle, and finally they may involve the entire skeletal system. Studies on the roentgenograms confirm the anatomopathologic observations and show that there exist three forms of cancerous skeletal lesions: (1) the osteoclastic or osteoporotic form, (2) the osteoplastic or osteoconstructive form and (3) the mixed form. The conditions under which the painful symptoms make their appearance differ. The cancer of the breast may or may not have been treated. The general condition of the patient may be florid or cachectic. The florid condition is surprisingly frequent in these patients. The onset of the painful syndrome may be insidious, under the form of slight, fleeting attacks; it may be abrupt, in the form of "rheumatismal" crises, or it may be sudden and persistent. The character of the painful syndromes varies with the localization of the cancerous metastases. The patients complain of pains in the back, in the shoulders or in the hips. The author gives detailed descriptions of these syndromes and in the conclusion he points out that these painful syndromes develop more frequently than formerly. He thinks that this might be due to the fact that the present day treatment of mammary cancer augments the rate of survival for these patients. On the other hand, it may only have the appearance of an increased frequency, because more cases are recognized now than formerly.

Monatsschrift f. Geburtshilfe u. Gynäkologie, Basel

108: 125-180 (July) 1938

*Mongolism. E. Kehrer.—p. 125.

Stereoscopic Roentgenoscopy for Localization of a Lost Intra-Uterine Pessary. H. Hellendall.—p. 143.

Teniasis as Cause of Uncontrollable Hypertremes Gravidarum. R. Oehlke.—p. 153.

Experiences in Care for Premature Birth. H. Volz.—p. 158.

Mongolism.—Kehrer describes four cases of mongolism in newborn infants and one of the extremely rare cases of familial mongolism. The manifestations of the developmental disturbances in the brain are already so pronounced in the newborn

infants that a diagnosis is possible without difficulty. In addition to the more or less characteristic facial expression, the following symptoms are of diagnostic significance: general muscular hypotonia, cutis laxa which is present chiefly on the occiput and on the back of the neck, immobility, somnolence and apathy, and the shortness and inward curvature of the terminal phalanges of the fifth fingers (Siebert's sign). The diencephalic-adenohypophyseal system may be involved in the developmental anomaly of the brain. This results in endocrinopathies, which may exist at birth but which do not become manifest until later. The observation of some authors that mongoloid children are usually borne by mothers who have passed the age of 40 was corroborated in only one of the four newborn. The author thinks that mongolism is caused partly by impairment of the germ plasma (ovum or spermatozoon), partly by damage to the embryo. In one of the four cases the mother had passed through an epidemic encephalitis two years before the birth of the child. In another case, consanguinity in the distant ancestry may have played a part.

Schweizerische medizinische Wochenschrift, Basel

68:981-1004 (Aug. 20) 1938. Partial Index

Surgical Foundations and Principles in War Medical Service of Switzerland. Dubs.—p. 981.

Focal Infection, Rheumatism and Short Wave Therapy. J. von Ries.—p. 989.

Adhesive Plaster Bandage as Substitute for Ligament in Lesion of Tibial Collateral Ligament of Knee. T. Johnner.—p. 990.

Technic of Air Filling of Joints. R. Meyer-Wildisen.—p. 991.

*Treatment of Morbus Maculosus Werlhofii. E. Jacobson.—p. 991.

Treatment of Morbus Maculosus Werlhofii.—Jacobson says that essential thrombopenia, which is better known under Werlhof's term "morbus maculosus," still presents a therapeutic problem. Most of the treatments that have been employed, such as blood transfusion, roentgenotherapy, protein therapy, various styptic preparations and vasoconstrictive remedies, are merely temporary, palliative measures. In the severe cases splenectomy is employed. As one of the reasons why there is as yet no satisfactory treatment, the author regards the fact that the cause of morbus maculosus werlhofii is not known. After citing some of the theories that have been advanced with regard to the cause, he points out that thrombopenia is one of the chief symptoms but that an important role has been ascribed also to the behavior of the vessels, particularly the capillaries. He resorted to treatment with phenylhydrazine for the first time in 1931. The favorable results obtained in the first cases induced further trials with this treatment. In all, it was employed in twenty-eight cases. The expectation that the phenylhydrazine would increase the number of thrombocytes was not realized, but in spite of this it produced improvement and thus fulfilled the purpose of the medication. In this connection it is pointed out that even after splenectomy the number of thrombocytes remains quite low. In some cases in which there was at first no therapeutic response to the phenylhydrazine the treatment was repeated several weeks later. Lack of tolerance or undesirable secondary effects were never observed. Phenylhydrazine hydrochloride was given during meals in doses of 0.1 cc. (enclosed in gelatin capsules). The total dose varied between 0.7 and 1.5 cc. Discussing the results of the treatment, the author says that in nineteen of the patients, the hemorrhagic tendency disappeared. This cure has so far persisted for from three to seven years. The other nine patients could not be traced.

Minerva Medica, Turin

2: 85-108 (July 28) 1938

*Fourth Derivation in Electrocardiography. F. De Matteis.—p. 86.

Nephropathy in Course of Brill's Disease. S. Dini.—p. 92.

Hemolytic Jaundice with Increased Globular Resistance. F. Rietti.—p. 95.

Fourth Electrocardiographic Lead.—De Matteis describes the fourth derivation as that obtained by placing a "different" electrode at the left frontal wall of the thorax and an "indifferent" one at either the posterior wall of the thorax (opposite to the "different" electrode) or at the left arm or leg. He obtained electrocardiograms in the fourth derivation by placing the "different" electrode on the left parasternal region and the indifferent electrode at the left arm. He observed the behavior

of the fourth derivation in 700 electrocardiograms of 207 persons. The group included normal persons and patients who were suffering from either adenoids or diseases of the heart. He found that the electrocardiogram which is taken in the fourth derivation in normal persons is normal in all cases. The pathologic changes of the fourth derivation electrocardiogram show involvement of the ventricular myocardium and of the coronary system in some cases of angina pectoris in which the electrocardiograms which are taken by the peripheral derivations are normal. Alterations of the fourth derivation in association with those of the peripheral derivations are of value in confirming the clinical diagnosis of myocardial infarct and determining the seat of the infarct. A pathologic fourth derivation does not show, specifically, myocardial infarct from coronary thrombosis. It may appear in compensated or decompensated insufficiency of the mitral valve, aortitis, total arrhythmia, myocarditis with generalized arteriosclerosis, acute rheumatic myocarditis, exophthalmic goiter and poisoning from digitalis. It shows functions of certain zones of the ventricular myocardium and of the coronary system which are not registered by the peripheral derivations.

Rassegna d'Ostetricia e Ginecologia, Naples

197-244 (May 31) 1938

*Nonspecific Protein Treatment in Inflammation of Female Internal Genitalia. G. Amabile.—p. 199.

Reticulocytosis and Tuberculosis in Obstetrics and Gynecology. G. Bezzi.—p. 209.

Protein in Inflammation of Female Genitalia.—Amabile administered injections of 5 cc. of boiled cow's milk to fourteen patients who had inflammations of the internal genitalia. Determinations of the leukocytes and of the leukocytic formula were made before and twenty-four and forty-eight hours after administration of the injection. The author found that the injection is followed by increase of the temperature and of the number of leukocytes, and diminution of the neutrophilic leukocytes and increase of the lymphocytes. The reaction lasts from twenty-four to forty-eight hours. Lymphocytosis permanently increases as the patient improves. According to the author, heterologous protein therapy stimulates a special reaction of the lymphocytes and improves the circulation of the lymph with consequent transportation of antibodies to the inflamed tissues. Increase of the lymphocytes after heterologous protein therapy shows a reaction of the body which induces favorable changes in the clinical evolution of the local inflammation, especially in puerperal infection. In the course of the latter, the sooner the administration of the treatment the better the results. The treatment is easily administered, is harmless and is well tolerated by the patients.

Revista de la Asoc. Med. Argentina, Buenos Aires

52: 551-610 (June 30) 1938. Partial Index

*Generalized Osteochondrosis. M. Gamboa and A. A. Salvati.—p. 551.

Phlebitis and Gonococcal Rheumatism. A. J. Heidenreich and G. C. Bertani.—p. 557.

Acute Yellow Atrophy of the Liver. A. Lopez Garcia, N. Quirno, A. Gorodner and R. Laticenda.—p. 559.

Associated Cancer and Tuberculosis of Mammary Region. E. A. Votta.—p. 568.

Annular Granuloma. M. A. Mazzini and J. R. Calcarami.—p. 571.

Chronic Urticaria. M. A. Fernandez and A. B. Storace.—p. 576.

Generalized Osteochondrosis.—Gamboa and Salvati studied a form of dystrophy of the bones, the so-called Morquio's disease, which was described for the first time by Morquio in the *Archives de médecine des enfants* 32:129 (Mareh) 1929 and abstracted in *The Journal* May 4, 1929, page 1560. Since then thirty-five cases have been reported in the literature. The disease has some similarity to osteochondritis, but it is not of an inflammatory origin. It is familial and sometimes hereditary. Generally the patients are children who develop normally until they begin to walk. At this time, and in the course of a few months, all the bones and large joints become permanently deformed. There is no pain during the process of deformation. The patient's head projects forward because of the presence of dorsal kyphosis. The root of the nose is slightly sunk and the eyes appear to be farther apart. The thorax clavicles are raised to the point of hiding the neck. The thorax becomes short and enlarged (barrel shaped) with the sternum

projected forward. The hip joint is in flexion and there is knock knee and flatfoot. The movements of the joints are either exaggerated or restricted. The muscles lack strength and the patients have the waddle of a duck. Roentgen examination shows processes of rarefaction deformation or destruction of the bones. The craniofacial diameters are slightly diminished and the sella turcica is greater than normal. The amount of calcium and phosphorus in the blood is either normal or increased. In the majority of cases the mentality is normal and the Wassermann reaction is negative. As age advances the anatomic lesions of the bone improve but the deformities are irreversible. Either consanguinity or endocrine disturbances have been considered the pathogenic factors of the disease. Syphilis, alcoholism and toxic infections seem to play no pathogenic role. The disease can be easily differentiated from other forms of bone diseases. Up to now endocrine treatment has failed. The actual aim is to prevent further deformities by an early diagnosis and care of the patient all through the process of ossification. At this time the progress of the disease stops. Orthopedics seems to be advisable in correcting deformities, but up to the present time it has not been resorted to. The author reports a case, the thirty-sixth in the literature.

Archiv für klinische Chirurgie, Berlin

192: 245-544 (July 9) 1938. Partial Index

- *Relations Between Economy of Body Heat and Surgical Intervention in Human Subjects. H. J. von Brandis.—p. 245.
- *Treatment of Neuralgia of Trigeminal Nerve by Means of Alcohol Injection into Gasserian Ganglion. H. von Brücke.—p. 328.
- Claudication Venosa of Upper Extremity as Symptom. M. Zehnder.—p. 354.
- Physiologic Significance of Gastrogram. S. Tagita.—p. 383.
- Cholecystography. H. Akaiwa and H. Komori.—p. 405.
- Occult Perforation of Gastroduodenal Ulcer with Spontaneous Cure. W. Klostermeyer.—p. 436.
- Action of Chordotomy on Spontaneous Gangrene. K. Sasaki.—p. 448.

Body Heat and Surgical Intervention.—It is pointed out by von Brandis that the undisturbed process of the vital functions of the human or animal organisms depends on a definite temperature. In this extensive report he describes his investigations on the body temperature before, during and after surgical interventions. He made these studies in order to gain insight into the thermoregulation of persons receiving surgical treatment. In view of the close connection between all functions under vegetative regulation, it was to be expected that under the influence of the surgical treatment the heat economy of the body would undergo changes similar to those that are known to occur in the circulation and the metabolism. Summarizing his observations, the author states that in surgical interventions which are made under general anesthesia the regulation of the body temperature is greatly impaired; in those made under spinal anesthesia it is partly subdued and in those under local anesthesia it is not impaired and may even be stimulated. Under general and spinal anesthesia, these changes become manifest in a noticeable subsidence in the heat formation, that is, in a cooling of the nuclear temperature, as well as in disturbances in the giving off of heat, in that it is increased in the peripheral regions of the skin. In interventions under local anesthesia the stimulation of the thermoregulation becomes manifest in a mild increase in the nuclear temperature, whereas the giving off of heat is not changed. The author emphasizes that under general and spinal anesthetics the thermoregulation is only subdued, not completely excluded. He observed that even under deep narcosis the regulation of the discharge of heat will become operative again at the moment when this becomes necessary in the interest of the organism on the whole. The author regards as especially important the observation that the aforementioned methods of anesthesia act differently on the heat regulation only so far as they are means to induce general, spinal or local anesthesia. The numerous substances that are available to produce any of these three types of anesthesia differ among themselves in their action on the thermoregulation only in degree. The author thinks that here the different toxicities are decisive. In the same way the impairment of the thermoregulation differs according to the condition of the patient; that is, his resistance to the operation and the type and location of the disorder as well as the extent of the intervention. The

parallelism in the behavior of circulation, metabolism and thermoregulation, that is, of the functions that are under vegetative regulation, is so complete that the effects of surgery and anesthesia appear at the same time and in the same form in all of them. The thermoregulation with its extraordinary constancy suggests that it might have a predominating position over some of the other functions that are under vegetative regulation. The author concludes that the continuous observation of the entire economy of body heat, that is, of the production as well as the discharge of heat, gives such reliable information about the vital functions before, during and after surgical interventions that the results are not only of scientific interest but also of clinical value.

Treatment of Trigeminal Neuralgia.—Von Brücke says that at the surgical clinics in Vienna and Graz trigeminal neuralgia is treated by means of the injection of alcohol into the gasserian ganglion. The injections are made under roentgenologic control, that is, the foramen ovale is demonstrated by means of roentgenography. The foramen ovale can be roentgenologically demonstrated without difficulty on axial exposures of the cranial base, but such exposures are of no practical value for reaching the gasserian ganglion by means of the puncture needle. It was found that the direction of the rays had to be identical with the direction of the needle. This direction has been designated by Härtel as the trigeminal axis; it passes from the trigeminal impression on the anterior surface of the pyramid in the direction of the third branch and through the center of the foramen ovale. Since the success of aimed roentgenograms depends largely on an exact adjustment of the x-ray tube, von Brücke devised an aiming apparatus. He describes this aiming apparatus, which is used not only for the adjustment of the x-ray tube but for the introduction of the needle into the foramen ovale. After the needle has reached the foramen the position is again controlled by roentgenoscopy. The injection is made with 90 per cent alcohol, which is given in small successive amounts of 0.2 cc. each. The total amount injected in one session varies between 0.6 and 1.5 cc.; more than 2.5 cc. should never be injected at one session. The author says that alcohol injection of the gasserian ganglion should be resorted to only in severe cases of true idiopathic trigeminal neuralgia and not until the usual conservative methods, including alcohol injections into the peripheral nerves, have been exhausted. He evaluates the results that have been obtained in twenty-five cases. He concludes that the alcohol injection into the gasserian ganglion under roentgenologic control is a reliable method which, because it is not dangerous, should be retained in spite of the improvements in the surgical interventions for trigeminal neuralgia.

Klinische Wochenschrift, Berlin

17: 1097-1136 (Aug. 6) 1938. Partial Index

- Studies on Substances with Antithyroid Action. E. Keeser.—p. 1100.
- Color Reactions and Chemical Methods of Determination for Gonadal Hormones. W. Zimmermann.—p. 1103.
- Vitamin A Content of Blood in Diseases of Liver. F. Lasch.—p. 1107.
- Quantitative Determination of Chief Urinary Pigments with Pulfrich Photometer. A. Sato.—p. 1108.
- Vitamin C Deficiency. A. Meyer.—p. 1111.
- Rare Occurrence of Adenocarcinoma of Cervix Uteri in Exophthalmic Goiter: Hormone Relations Between Ovaries, Thyroid and Carcinoma. B. Belonoschkin.—p. 1117.
- *Bitterlings for Testing Male and Female Sex Hormones. E. Glaser and F. Ranftl.—p. 1120.

Bitterlings for Testing Sex Hormones.—Glaser and Ranftl criticize studies recently reported by Duyvené de Wit and emphasize that the growth of the ovipositor of female bitterlings belongs to those secondary sex characters which can be influenced by female as well as by male hormones; the female hormone merely has a somewhat more pronounced effect on the growth of the ovipositor. Otherwise it may be assumed that here, as in the Allen-Doisy test, the sex hormones of various structures (estrone, beta-estradiol, estriol, equilin, equilenin and so on) will show quantitative variations, which can be observed also during the different seasons. If these peculiarities of the ovipositor test on bitterlings are taken into consideration, the test can be used, although not alone, at least as a corroborating test in addition to other tests, for certain clinical purposes. The authors think that contradictory reports in the literature find their explanation in the fact that the investigators put

especial stress on one or on another property. Regarding the "wedding dress" of the male bitterling, the authors maintain that it is the best test for the male hormone. It is not only cheap and simple but it has a degree of sensitivity that is reached by no other biologic test for the male sex hormone. The physiologic actions of progesterone correspond to a large extent to those of the so-called pure male sex hormones. Thus progesterone produces the "wedding dress" in male bitterlings, but it also increases the growth of the ovipositor in female bitterlings. If administered to mice during the phase of proliferation, progesterone prolongs the cycle; if administered during the secretory phase, it hastens the onset of estrus. The combined administration of male and female hormones shows additive effects in the ovipositor test on female bitterlings, but in the "wedding dress" of the male bitterling the antagonistic action of male and female hormones becomes evident; if sufficiently large quantities of female hormones are added, the male hormone remains ineffective.

Zeitschrift f. d. ges. Neurol. u. Psychiatrie, Berlin

162: 1-168 (July 21) 1938

Hereditary Pathology of Manic-Depressive Insanity: Parents and Children of Patients with Manic-Depressive Insanity. E. Slater.—p. 1.
Insanity and Death of Paranoid Mass Murderer Wagner: Epicrisis. R. Gaupp.—p. 48.

*Acute Multiple Sclerosis. H. Kreissel.—p. 83.

Drawings of Patient with Total Aphasia. A. A. Boon and P. Feitscher.—p. 103.

*Apoplectic Onset of Disorder in Case of Cerebral Tumors. A. Stender.—p. 123.

Acute Multiple Sclerosis.—According to Kreissel, the differentiation of acute multiple sclerosis from disseminated encephalomyelitis still awaits clarification. Whereas some classify acute multiple sclerosis and even multiple sclerosis with disseminated encephalomyelitis, others maintain that acute multiple sclerosis is a typical multiple sclerosis with an especially acute course. The author thinks that, as long as the etiology is not yet completely explained, a differentiation can be based only on clinical and anatomic aspects. He describes anatomic studies on the brain and the upper portion of the cervical spinal cord of a patient who died following acute multiple sclerosis. He emphasizes the changes that are identical with those of multiple sclerosis, particularly as regards their localization. He gives a detailed description of a peculiar, border-like process on the periphery of the cerebral peduncles, of the pons and of the medulla oblongata and compares this process with similar ones that have been described in the literature. He was able to detect some similarities with the encephalitis that develops after measles or after vaccination. Nevertheless, he shows that disseminated encephalomyelitis can be differentiated from the encephalomyelitis that develop after measles and vaccination as well as from acute multiple sclerosis. In the histopathologic picture of disseminated encephalomyelitis, the inflammatory infiltrative process predominates; however, in that of the encephalomyelitis after measles and vaccination, the inflammatory infiltrative reactions are much less severe than the proliferations of the glia. The described case is characterized by the acute disintegration of the medullary sheaths; this is much more noticeable than the inflammatory reaction on the vessels. In view of the disintegration of the medullary sheaths and of the localization of the processes, the diagnosis of acute multiple sclerosis was regarded as justified. The clinical aspects of the case were like those of multiple sclerosis.

Apoplectic Onset in Cerebral Tumors.—Stender reports twelve cases of cerebral tumor which began with an apoplectic attack and subsequent hemiplegia. In the majority of the cases the apoplexy appeared suddenly, but in some cases unsuspected prodromal symptoms preceded it. The clinical picture immediately after the apoplectic attack was usually that of an extensive or even of a complete exclusion of the corticospinal tracts of the involved hemisphere; that is, there was hemiplegia and hemianesthesia and in several instances there existed in addition a hemianopia and an aphasia. Objective signs of cerebral pressure, particularly choked disk, were lacking in the majority of cases, but in several patients the pupillary reactions were disordered. With one exception, all of the cases terminated in death and the majority of patients survived only a comparatively short time after the apoplectic attack. Thus

the prognosis is unfavorable in the cases of cerebral tumor which begin with an apoplectic attack. After citing the localization of the tumors and the histologic aspects, the author discusses the pathogenesis. He regards hemorrhages from a ruptured vessel of the tumor or malacia by vascular occlusion from the pressure of the tumor as possible causes of the apoplectic attack. However, postmortem observations indicated that in the majority of cases an acute cerebral edema was the direct cause of the apoplectic attack.

Vestnik Khirurgii, Leningrad

55: 223-372 (March) 1938. Partial Index

Vascular Reaction of Isolated Organ in Traumatic Shock. S. I. Banaytis.—p. 225.

Combined Roentgen Neurosurgical Therapy of Salivary Fistula of the Parotid Gland. N. N. Sokolov.—p. 243.

Anatomy and Surgery of Thoracic Duct and Roentgenography of Lymphatic System. L. A. Zhdanov and V. M. Durnashkina.—p. 246.

Latent Infection After Herniotomy. F. B. Kheyne-Kheyfets.—p. 284.

Dermoid Cyst of the Rectum. Ya. Ya. Dzhanelidze.—p. 289.

Temporary Prosthesis of Bilateral Stumps of Upper Extremities. Ya. I. Luric.—p. 302.

*Segmental Osteotomy. A. S. Pertsovskiy.—p. 307.

Multiple Segmental Osteotomy.—According to Pertsovskiy the various methods of osteotomy thus far proposed failed to solve the problem of actual elongation of the limb. The inadequacy of the methods is even more evident when in addition to the lengthening of the extremity it becomes advisable to correct its position. The multiple osteotomy method of Bogoraz is capable of accomplishing both results. It is applicable in cases of angular ankylosis as well as in cases of ankylosis of the femur in the hip joint with the extremity in extension. In addition the method is capable of accomplishing actual lengthening of the limb without altering the relations in the hip joint. The author's roentgenograms demonstrate that, as the result of traction by a Kirschner wire through the diaphysis, the bone segments in this operation become separated from the upper fragment and the lower fragment of the femur as well as from one another by a distance of from 2 to 3 cm. and that they are maintained in proper alignment. The greatest elongation obtained by the author amounted to 9 cm.

Nederlandsch Tijdschrift v. Geneeskunde, Amsterdam

82: 3719-3822 (July 30) 1938. Partial Index

*Course of Experimental Tuberculosis in Castrated and Noncastrated Animals. C. van Bokkum.—p. 3731.

Carriers of Typhoid Bacilli. H. Peeters, A. Charlotte Ruys and C. H. Ephraim.—p. 3741.

Technic of Radium Therapy of Uterus. D. M. Levy.—p. 3749.

Tuberculosis in Castrated and Noncastrated Animals.—According to van Bokkum, it has long been known that the chance of contracting tuberculosis differs in various periods of life. The period of puberty and the period of the height of the sex function (around the age of 30) are supposedly especially unfavorable. Animal experiments have been made to determine whether there are connections between the function of the sex glands and the tuberculous infection, but in many of these experiments the number of animals was rather limited, so that the author decided to employ a larger material to investigate the influence of castration on the susceptibility to tuberculosis. He made his studies on two series of animals. The first series consisted of five male and five female castrated guinea-pigs and of five male and five female guinea pigs that were not castrated; that is, in all, this series consisted of four groups of animals. The animals were inoculated with human tubercle bacilli the virulence of which had been tested previously on six guinea pigs. Five months had elapsed since the castration before the inoculations were made. In a second series of experiments the author again employed four groups of guinea pigs, but in this series the groups consisted of from seven to nine animals each and the inoculations with tubercle bacilli were made four months after castration. As regards neither the length of survival nor the anatomic dissemination of the tuberculous processes was it possible to detect differences in the various groups of animals. The author concludes from these observations that there is no reason to correlate the differences in the susceptibility for tuberculosis during the different periods of life to the gonadal function.

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UROLOGIC CONDITIONS SIMULATING CHRONIC GLOMERULONEPHRITIS

CHAIRMAN'S ADDRESS

A. J. SCHOLL, M.D.

LOS ANGELES

Since certain curable diseases of the urinary tract may simulate chronic glomerulonephritis, it is essential that such curable diseases are not overlooked. That they are occasionally overlooked even in the most advanced medical centers is attested by the words of O. H. P. Pepper.¹ He said: "We have had patients die in our hospital with a diagnosis of chronic Bright's disease of some type or other, to be horrified at autopsy that the condition was altogether a lower urinary tract obstruction with hydronephrosis, an obstructive lesion destroying the glomeruli just as effectually as glomerulonephritis does, giving impaired renal function."

UREMIA

Uremia is the most prominent symptom of patients who have chronic glomerulonephritis and of those who have a lesion of the urinary tract of an obstructive or infectious nature. It is observed frequently as a complication of nephritis, and for this reason unless patients with uremia exhibit obvious signs of pathologic change in the urinary tract they are thought to have chronic glomerulonephritis.

Any disease or injury whereby so much of the renal tissue is destroyed that the remainder is unable to compensate for the loss may cause uremia. Renal insufficiency does not develop if a small amount of normal parenchyma is left. The work of Tuffier² thirty years ago and that of Bobroff³ later demonstrated that life could be maintained if a very small portion of a normal kidney remained. Tuffier, in his experimental work, performed total unilateral nephrectomy plus more or less extensive resection of the other kidney in an endeavor to find the exact quantity of normal renal tissue necessary for the maintenance of life. He found that there was a definite regeneration of tissue in the remaining segment only when the portion allowed to remain was sound.

A number of early writers attempted to distinguish between the uremia associated with nephritis and the

uremia common to anuria. Ascoli⁴ in 1903 made two divisions: (1) urinary poisoning, in which the symptoms of the disease are similar to those found in anuria produced by mechanical means and are caused by retained metabolites and (2) renal uremia, characterized by sudden convulsive seizures, which he believed were caused by certain unrecognized nephrolyses. According to Fishberg,⁵ Widál arrived at a similar division from the point of view of blood chemistry. He found that in the clinical picture corresponding to Ascoli's urinary poisoning the amount of urea in the blood is increased and he therefore called it azotemia, believing that the symptoms were due to uremic poisoning. The acute convulsive type he termed chlor-uremia, on the assumption that the retention of chlorides caused the convulsive seizures.

Volhard⁶ combined the two conditions. He said: "When we compare the symptoms which appear only with renal insufficiency and which we have designated as symptoms of true uremia with those occurring in anuria, we find them almost identical."

The urologist considering uremia thinks of the retention of nitrogen in the blood associated with obstruction of the vesical neck or of that associated with calculous anuria. He attempts to relieve the obstruction, to subdue the infection or to drain the offending accumulation, and he considers the prognosis as at least not unfavorable. The internist considering uremia frequently thinks in the unfavorable terms of chronic nephritis. The rapidly fatal outcome of the disease in patients who have a high value for retention of nitrogen is constantly before him. Chace and Myers⁷ reported a series of cases in which the patients who had chronic glomerulonephritis associated with a value for retention of creatinine of more than 5 mg. per hundred cubic centimeters of blood died early in the course of the disease. In contrast to these figures, patients with obstructive lesions whose concentration of urea was from 80 to 100 mg. per hundred cubic centimeters of blood and whose values for creatinine were from 8 to 10 mg. usually recovered after proper treatment.

Rowntree,⁸ in discussing uremia, stated that sometimes by clinical methods only it is impossible to recognize whether the uremia is due to organic or to functional changes. The development of uremia in a case of marked chronic nephritis offers little in a permanent way as a result of treatment; whereas in the

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7. Chace, A. F., and Myers, V. C.: The Value of Recent Laboratory Tests in the Diagnosis and Treatment of Nephritis, J. A. M. A. 67: 929. 932 (Sept. 23) 1916.

8. Rowntree, L. G.: Practical Treatment, Philadelphia, W. B. Saunders Company, 1917, vol. 4, pp. 800-855.

presence of an identical clinical picture encountered in a case in which the kidney has been injured by back pressure, the prognosis may be good. Wohl and Brust,⁹ reporting uremia with conditions other than chronic glomerulonephritis, stated that the impression gained from a perusal of the literature, as well as from modern textbooks of medicine, is that an increase in the presence of nitrogenous waste products in the blood is indicative of chronic glomerulonephritis. The importance of recognizing these states clinically and early lies in the fact that many of them mistakenly are thought to be of renal origin, especially since traces of albumin and some casts are frequently found on examination of patients whose disease is not primarily of renal origin.

Ascoli⁴ stated positively that the uremia which he called urinary poisoning was quite different from that associated with chronic glomerulonephritis. The patient, as noted by Foster,¹⁰ who studied three patients whose only functioning kidney was removed surgically because of some disease, has few or none of the symptoms which mark the conception of spontaneous uremia. Convulsive seizures are rarely observed, nervous phenomena are conspicuously lacking, headaches are rare and vomiting only occasionally occurs. Foster stated that urinary poisoning is produced by some rather sudden change in the excretory organs, resulting in prompt flooding of the tissues with nitrogenous waste products. When failure of elimination is not so rapid and the waste products accumulate in the tissue fluids more gradually, it is conceivable that the cells acquire a certain degree of tolerance and are not so injured as they appear to be when the change is sudden.

The following case, previously reported by Scholl and Foulds, is one of anuria which resulted from a long-standing complete obstruction of a single functioning kidney. Involving an excessively high value for retention of nitrogen, this case illustrates the freedom from uremic symptoms and the clarity of intellect common to patients who have anuria, contrasting sharply to the stupor, anorexia and convulsions of those who have chronic nephritis.

CASE 1.—A woman aged 60, who complained of frequency of micturition and of dysuria, for three months had had dull intermittent pain in the left side of the abdomen and occasionally hematuria.

When first seen she was voiding small amounts of urine every half hour and had lost 20 pounds (9 Kg.) during the previous four months. The blood pressure in millimeters of mercury was 176 systolic and 106 diastolic. Examination of the eyegrounds gave negative results. A single specimen of urine had a specific gravity of 1.002; the urine was acid in reaction and contained a small amount of albumin, a few erythrocytes and many pus cells. There was no return of phenolsulfonphthalein in two hours. The concentration of urea was 130 mg. and that of creatinine 3.3 mg. per hundred cubic centimeters of blood. Neither ureteral orifice was seen on cystoscopic examination, although there was a scar of inflammation in the region of the left opening.

For sixteen days the patient voided from 400 to 1,200 cc. of urine a day. For the next fourteen days the only urine secreted was .25 cc., which was voided in a single day. Moderate edema of the eyelids appeared. Her appetite was poor and she vomited occasionally. Several days after the onset of anuria a mass became evident in the region of the right kidney. The concentration of blood urea gradually rose until it was 527 mg.

per hundred cubic centimeters of blood and the concentration of creatinine increased to 26.6 mg., and still she remained clear mentally and had no evidence of convulsions.

At exploration an obstructive hydronephrosis was found on the right side and an atrophic functionless kidney on the left. A decapsulation and pelviotomy were performed on the right kidney. After operation the patient's condition improved somewhat and the values for retention of nitrogen in the blood decreased markedly, but she died several days later.

In addition to diseases of urologic origin, there are a number of diseases of prerenal or extrarenal origin which cause excessive retention of nitrogenous elements in the blood and to a certain extent simulate chronic glomerulonephritis. These conditions, such as multiple myeloma, pyloric and intestinal obstruction, fevers and inflammation, acute poisoning by mercury, phosphorus, lead or turpentine and renal thrombosis and collapse after severe injuries or after operations, have been well reported elsewhere. Diabetes insipidus at times closely resembles nephritis, particularly when it is of moderate degree and occurs in early childhood. It is of interest that the first patient to whom Rowntree and Geraghty¹¹ gave the phenolsulfonphthalein test was a child suffering from diabetes insipidus, in whom they proved that the renal function was practically nil. At necropsy the case proved to be one of chronic nephritis.

This paper is concerned only with urologic conditions which simulate, and are at times confused with, chronic nephritis.

PYELONEPHRITIS

Pyelonephritis either alone or in association with some other lesion of the urinary tract most frequently resembles, and is most commonly confused with, chronic glomerulonephritis.

In its milder forms, pyelonephritis is seen frequently by the urologist in a form in which it causes few symptoms and only slight renal damage; it persists for years and is marked by more or less frequent exacerbations. It is almost invariably bilateral, and while it occurs usually without demonstrable or evident obstruction to the outflow of urine, it also is present in some degree in most cases of obstruction of the urinary tract and is a causative factor in progressive destruction of the kidney.

In the early stages of the disease the blood pressure is normal or at times slightly below normal. As the disease progresses and more and more renal damage occurs, the blood pressure rises. This is not, however, an invariable occurrence, as in three cases reported by Longcope,¹² wherein the patients died, the blood pressure remained normal. He stated that usually the blood pressure in such cases rises during the latter months or years of the presence of the disease and may reach such high figures as 225 mm. of mercury systolic and 150 mm. diastolic. The blood pressure was above 160 mm. systolic and 105 mm. diastolic in ten of fifteen cases observed by him during the terminal stages of the disease. In half of these cases the systolic pressure was 200 mm. or over, and in ten the diastolic pressure was between 110 and 150 mm.

On examination the eyegrounds usually are normal in the mild forms of the disease. In severe forms

9. Wohl, M. G., and Brust, R. W.: *High Blood Urea Nitrogen Not Due to Chronic Nephritis*, J. Lab. & Clin. Med. 20: 1170-1179 (Aug.) 1935.

10. Foster, N. B.: *Text-Book of Medicine*, ed. 3, Philadelphia, W. B. Saunders Company, 1934, pp. 965-969.

11. Rowntree, L. G., and Geraghty, J. T.: Personal communication to the author.

12. Longcope, W. T.: *Chronic Bilateral Pyelonephritis: Its Origin and Its Association with Hypertension*, Ann. Int. Med. 11: 149-163 (July) 1937.

occasional, usually single, hemorrhages or cotton wool patches may be found in the retina. Wagener¹³ stated that these patches are of the type seen in patients with general toxemia or septicemia of any origin and are not characteristic of the renal disease and are not related to the degree of renal insufficiency.

Glomerulonephritis is the only variety of nephritis in which retinitis is common. The retinitis associated with glomerulonephritis commonly is designated albuminuric retinitis; it is characterized by anemia and edema of the disk; generalized, rather dense edema of the retina, usually grayish white; hemorrhages and cotton wool patches, and, in the macular region, the radiating star figure made up of large, thick groups of hard white exudate. This picture is distinct, limited to cases of glomerulonephritis and never found in association with uncomplicated obstructive lesions of the urinary tract. On the other hand, patients with obstructive lesions of the urinary tract, especially those in whom infection is also present, may have chronic glomerulonephritis also, together with all the associated signs of this condition. Longcope¹² reported that three of nine patients who had chronic pyelonephritis and whose disease proved fatal had also associated a chronic diffuse glomerulonephritis.

The urine in cases of pyelonephritis usually is slightly cloudy and frequently shows the slight opalescence associated with bacteriuria characteristic of infections caused by *Escherichia coli*. The specific gravity of the urine is usually low and the urine contains a moderate amount of albumin, many leukocytes and more frequently than not a large number of bacteria. In an occasional case, if the disease is of long duration and the infection mild, when the infection is due to the coccus group, only small numbers of leukocytes may be present or none may be found, but almost invariably bacteria are plentiful in the sediment and positive cultures are obtained. Dr. Tinsdale Harrison¹⁴ demands repeated negative cultures in all cases in which the diagnosis is glomerulonephritis before he rules out infection of the urinary tract and accepts the diagnosis of nephritis. With regard to the urine, the most helpful fact in distinguishing pyelonephritis from chronic glomerulonephritis is that with the former casts are rarely and erythrocytes are only occasionally found. The amount of phenolsulfonphthalein returned is definitely lowered, even with the milder forms of the disease, especially during the periods of exacerbation. When the disease is of long duration, only 5 per cent or, occasionally, only a trace of dye is returned.

An examination of the blood usually reveals a reduction in the amount of hemoglobin, and, contrary to conditions found in the blood in cases of nephritis, there is an increase in the leukocyte count, further evidence of infection.

The concentration of nonprotein nitrogen in the blood is usually elevated above normal and is a good index of the degree of permanent renal damage. In one case, with a return of only a trace of phenolsulfonphthalein in two hours, the concentration of nonprotein nitrogen varied from 70 to 90 mg. per hundred cubic centimeters of blood, for more than two years. Values in excess of 100 mg. are not unusual.

The following case illustrates the difficulties in establishing a diagnosis of pyelonephritis and the similarity between its symptoms and those of chronic glomerulonephritis, as well as the help derived from establishing the correct diagnosis and instituting treatment:

CASE 2.—A man aged 52, who had been sick for four years, had lost 30 pounds (14 Kg.) in the last two years, had been weak and tired and had had frequent headaches. He had voided frequently at night and had occasionally had moderate dysuria.

On physical examination his blood pressure in millimeters of mercury was 160 systolic and 105 diastolic. His expressed prostatic secretion contained a large amount of pus. His blood contained 48 per cent of hemoglobin; the red blood cell count was 3,200,000 and the leukocyte count 12,500. The urine was pale and slightly cloudy and had a specific gravity of 1.007. It contained many leukocytes and bacteria but no casts or erythrocytes. Culture of the urine from the kidney and the bladder yielded *Escherichia coli*. The two hour return of phenolsulfonphthalein was 10 per cent. The concentration of nonprotein nitrogen was 60 mg. per hundred cubic centimeters of blood.

Repeated lavage of the renal pelves; irrigation of the bladder and prostatic massage were carried out, together with the administration of urinary antiseptics. In four months he had gained 20 pounds (9 Kg.), the concentration of nonprotein nitrogen had dropped to 42 mg. per hundred cubic centimeters of blood and the return of phenolsulfonphthalein had increased to 25 per cent in two hours. The urine was much clearer, and he felt in general greatly improved.

He was not seen again until eighteen months later. He had had no treatment in the meantime and most of his symptoms had recurred. He again had lost considerable weight. The systolic blood pressure was 180 mm. of mercury, and the urine contained many leukocytes and bacteria. The return of phenolsulfonphthalein was less than a trace in two hours, and the concentration of nonprotein nitrogen was more than 100 mg. per hundred cubic centimeters of blood on two occasions. No treatment was given at this time.

In this case a number of conditions were suggestive of chronic nephritis—high nitrogen retention, increased blood pressure, and low phenolsulfonphthalein output. The diagnosis was definitely established by data obtained by laboratory examination, by cystoscopy and by the response to treatment as a urinary tract infection. *Escherichia coli* was present in the pelves of both kidneys; the urine contained no casts or erythrocytes and only a small trace of albumin, but many leukocytes, and the blood showed an increased number of leukocytes, evidence of an infectious process.

In an occasional case the various diagnostic features may not be so prominent, and it may be impossible definitely to state that the condition is not pure nephritis; or, as previously stated, the two conditions may overlap.

OBSTRUCTION OF THE UPPER PART OF THE URINARY TRACT

Complete or partial anuria results when the two kidneys are blocked simultaneously, when the ureter to a single kidney is obstructed or when the better of the kidneys is blocked and the other is overloaded. In contrast to the anuria associated with nephritis, the anuria associated with obstruction of the ureter is striking because of the mildness of the early symptoms. The individual patient may continue to enjoy health for several days in spite of voiding only a few centimeters of urine daily. Later preuremic symptoms, such as hiccuping, vomiting and muscular twitching, develop. Rarely is there difficulty in arriving at a diagnosis in

13. Wagener, H. P.: *The Kidney in Health and Disease*, Philadelphia, Lea & Febiger, 1935, pp. 622-637.

14. Harrison, Tinsdale: Unpublished clinicopathologic discussion, California State Medical Society General Meeting, May 9-11, 1935.

cases of acute obstructive anuria. The previous history of the patient and the associated localized pain suggest the condition present and indicate the need for roentgenographic and urologic investigation. It is the long-standing ureteral obstruction of moderate degree that is not correctly diagnosed and that may be confused with nephritis. Chronic bilateral ureteral obstruction of even moderate severity is usually associated with some infection and at times the picture is one more of infection than of obstruction, but usually it is a combination of the two conditions. On the other hand, extensive destruction of the renal parenchyma rarely occurs from infection alone, without some degree of obstruction of the urinary tract being present.

The association of pressure, atrophy and infection results in renal insufficiency. The picture, especially if the patient is young, is sometimes very similar to that of chronic glomerulonephritis. There are several features which aid in distinguishing the two conditions. Examination of the eyegrounds usually reveals nothing abnormal in cases in which the obstruction appears early in the course of the disease. Even in cases in which the obstruction appears late or is severe, rarely is anything found except the occasional retinal hemorrhage seen in cases of general toxemia. Such hemorrhage is markedly in contrast to the albuminuric retinitis associated with chronic glomerulonephritis. The urine, similar to that seen in cases of pyelonephritis, contains many leukocytes and bacteria, only occasionally casts or erythrocytes and only small quantities of albumin. The blood shows evidence of infection by an increased leukocyte count. The most significant difference between these two conditions is that the patient who has obstruction, even though he exhibits marked retention of nitrogen in the blood, is not as sick as the patient who has chronic glomerulonephritis associated with a similar concentration of urea in the blood. The patient who has obstruction of the ureter is frequently ambulatory and complains only of anorexia, headache and some dizziness; in contrast, the patient who has nephritis is bedfast and stuporous and has convulsions.

The following case is that of a young woman whose condition was diagnosed and treated as glomerulonephritis but was found at necropsy to be bilateral congenital obstruction of the ureter and dilatation of the upper part of the urinary tract:

CASE 3.¹⁵—A woman aged 21, who complained of loss of strength and endurance for one week, four years before had been told that she had Bright's disease. At that time she had lost her sight and had albumin in the urine and her blood pressure was 240 mm. of mercury. She gradually had improved and had been able to do some work until one week before she came for examination.

Some edema of the face and neck was present. Examination of the eyegrounds disclosed numerous areas of pigmentation that were thought to indicate scars due to old hemorrhages. The vessels were more sclerotic than normal. The blood pressure in millimeters of mercury was 188 systolic and 120 diastolic. The urine contained large numbers of leukocytes and a large amount of albumin but no casts and only rarely an erythrocyte. The specific gravity was 1.014. The concentration of hemoglobin was 41 per cent; the red blood cell count was 2,300,000 and the leukocyte count 11,100. The concentration of nonprotein nitrogen was 133 mg., that of urea 113 mg. and that of creatinine 8.5 mg. per hundred cubic centimeters of blood. With rest in bed and a high caloric, high vitamin and low salt diet the patient became steadily worse and died.

15. Drs. B. O. Raulston and E. M. Butts permitted me to use the details of this case.

Necropsy revealed congenital dilatation of the ureters, with almost complete obstruction at the point where they passed over the brim of the pelvis; bilateral hydronephrosis; acute pyelonephritis, and cystitis.

There are a number of points in this case suggesting the true nature of the condition present, infection of the urinary tract. The leukocyte count in the blood was elevated; there were no erythrocytes or casts in the urine, but there were large numbers of bacteria. The eyegrounds did not have the features associated with chronic glomerulonephritis and showed merely the retinitis associated with hypertension. Finally, a patient who had chronic glomerulonephritis and in whose blood the concentration of nitrogen was similar to that of this patient would be prostrated, possibly comatose, or would have convulsions.

OBSTRUCTION OF THE LOWER PART OF THE URINARY TRACT

Obstruction of that part of the urinary passage which lies below the bladder results most frequently from prostatic hypertrophy, carcinoma, contracture of the neck of the bladder or urethral stricture. Any of these conditions may cause retention of urine, back pressure and renal insufficiency.

For the purpose of this report it makes little difference what the cause of the obstruction may be; the effect on the upper part of the urinary tract is the same. In the early stages of prostatic obstruction, the most common cause of retention of urine in men, increased frequency of contraction of the trigon in attempts to open the vesical orifice causes compression and obstruction of the lower part of the ureter. Obstruction below and peristaltic pressure above result in ureteral and later in pelvic distention. Later there may occur incompetence of the ureterovesical valve, which permits ureteral regurgitation and which converts the bladder, ureter and renal pelvis into one connecting waterway under variable pressure. With dilatation of the pelvis and calices, thinning of the renal cortex and impairment of function result.

With renal impairment, symptoms of uremia appear. If there is also present an infection of part of the urinary tract and more or less pyelonephritis, the symptoms of renal impairment and uremia progress much more rapidly.

In an occasional case the symptoms due to renal embarrassment outweigh the local symptoms of obstruction. The patient may not have definite symptoms of disease of the bladder or he may not include symptoms of disease of the urinary tract among his leading symptoms. This is frequently seen in cases of slow-growing, malignant, prostatic obstruction.

In one case the only complaints were dizziness, nausea and loss of weight. The concentration of nonprotein nitrogen was 110 mg. per hundred cubic centimeters of blood. There was no frequency, nocturia or pain. The patient thought that urination was normal. The prostate gland was small, smooth and fibrotic. The fact that it was fixed, firm and stony gave definite evidence of cancer of the prostate and indicated that disease of that organ was responsible for the condition. A rounded smooth mass, recognized as a distended bladder, could be felt above the pubis. Catheterization revealed retention of 1,000 cc. of urine, promptly relieved the symptoms and permitted the amount of nitrogen in the blood to return to normal.

The large amount of nitrogen retained in the blood in such cases may not be due entirely to renal insufficiency. The work of Fender¹⁶ has shown that the mucosa of the bladder when inflamed transmits urea in quantities sufficient to raise appreciably the concentration of nonprotein nitrogen in the blood. If the bladder is normal this does not occur. On the other hand, in most cases in which there is retention of urine in the bladder for long periods there is some mucosal inflammation. In one patient who had residual urine in excess of 600 cc., the concentration of nonprotein nitrogen was in excess of 90 mg. Twenty-four hours after a permanent urethral catheter was inserted the concentration of nonprotein nitrogen was less than 50 mg. Removal of the catheter, permitting retention to recur, caused the concentration of nonprotein nitrogen to return in twenty-four hours to more than 80 mg. Insertion and removal were done on several occasions and caused similar, but smaller, excursions of retention of nitrogen with each trial.

Uremia develops very readily in infants and children if obstruction is below the bladder. The symptoms are more severe and the disease is more rapidly fatal than if obstruction is in the upper part of the urinary tract. Campbell¹⁷ stated that the symptoms and the results of laboratory examination in the preuremic stage of the disease in cases of urinary obstruction in children may not be distinguishable from those of chronic nephritis.

Campbell reported the case of a boy aged 14 months who had bilateral hydronephrosis secondary to congenital hypertrophy of the verumontanum. A diagnosis of chronic nephritis was made. The urine had a low specific gravity and contained albumin and hyaline and granular casts, and the concentration of nitrogen in the blood was increased. The true nature of the condition was noted at necropsy.

In a second case reported by Campbell,¹⁷ that of a girl aged 8 years, a diagnosis of chronic nephritis was made from the laboratory examination. The child was observed for eighteen months, during which time the blood pressure rose from 140 to 230 mm. of mercury. Three months before death occurred, cystoscopy revealed a bilateral ureteropelvic obstruction and hydronephrosis; these conditions were confirmed subsequently, at necropsy.

The diagnosis of most of the obstructive lesions of this type is determined by examination of the urinary tract; if this is carried out, usually there is no particular difficulty in ruling out nephritis. The urine in most cases of obstruction contains many leukocytes, small amounts of albumin and only rarely erythrocytes or casts. In the occasional case of obstruction in which the urine is not affected, the absence of casts or erythrocytes and the slight amount, or absence, of albumin are important diagnostic leads.

Patients who have uremia due to obstructive lesions are seldom likely to have convulsions, although they may have muscular twitchings. They are not very sick, and in general most of their symptoms are less pronounced than are the symptoms of patients who have chronic nephritis and a similar high retention of nitrogen.

POLYCYSTIC RENAL DISEASE

The clinical picture of impaired renal function, hypertension and hematuria in cases of polycystic disease is very similar to that associated with chronic glomerulonephritis, and the diseases are not infrequently so diagnosed. Symptoms of gastrointestinal disorders, such as loss of appetite, nausea and vomiting, are not uncommon, and anemia, headache and weakness may occur. Examination of the urine reveals that it is not unlike that seen in cases of chronic nephritis. The specific gravity is frequently less than 1.010, albumin is always present and erythrocytes may be found. Casts are found in only a small percentage of cases.

A definite impairment of renal function usually occurs before a physician is consulted. There are a decreased output of phenolsulfonphthalein, retention of nitrogenous substances in the blood and decreased ability to concentrate urine. The return of phenolsulfonphthalein was less than normal in 67 per cent of 193 cases reported by Braasch and Schacht.¹⁸ In some of their cases no dye, or only a trace, was secreted. In 67 per cent of 117 of their cases in which the determination of nitrogen was noted, the concentration of urea was more than 40 mg. per hundred cubic centimeters of blood, and in only thirty-three was it normal; in twelve cases it was more than 200 mg. Hypertension occurs early and is usually present when the disease is advanced; cases in which the systolic blood pressure varies from 170 to 200 are not uncommon.

Sclerosis of the retinal arterioles is seen at times; this is of the type usually seen in cases of essential hypertension, and when retinitis occurs it is not different from the retinitis associated with essential hypertension. It usually can be distinguished from the retinitis associated with chronic glomerulonephritis. It is retinitis associated with hypertensive disease and not retinitis associated with nephritis, although the hypertension probably arises as a sequela of the renal lesion.¹³

Differing from patients who have acute obstruction of the lower part of the urinary tract and also from those who have chronic glomerulonephritis, many who have polycystic renal disease have acquired a remarkable tolerance to renal insufficiency. Even if the concentration of blood urea nitrogen is in excess of 150 mg. per hundred cubic centimeters, even if the value for blood creatinine is from 5 to 8 mg. and even if no more than a trace of phenolsulfonphthalein is returned in the urine, patients not infrequently are able to live in comparative comfort for years. Similar signs of a high concentration of nitrogen in the blood if a patient had chronic glomerulonephritis would suggest rapid death.

On account of the insidious onset of polycystic renal disease and the physical accommodation to the condition that has just been mentioned, many patients are not aware of its presence until almost complete destruction of the kidney has occurred. Death is usually due, as with chronic glomerulonephritis, to renal insufficiency, often markedly increased by associated infection of the renal pelvis, which if untreated hastens the process of destruction of tissue. Control of the urinary infection by proper drainage and the administration of urinary antiseptics will do much toward retarding the progress of the usually steadily advancing parenchymal destruction. Regulation of the patient's manner of living, and

16. Fender, F. A.: Absorption of Urea from the Bladder. *Arch. Surg.* 25: 180-188 (Jan.) 1934.

17. Campbell, M. F.: *Pediatric Urology*, New York, Macmillan Company, 1937, vol. 1, p. 151.

18. Braasch, W. F., and Schacht, F. W.: Pathologic and Clinical Data Concerning Polycystic Kidney. *Tr. Am. A. Genito-Urin. Surgeons* 25: 85, 1932.

dietary precautions, including restriction of intake of protein, may help considerably.

In an occasional case, surgical intervention may help to limit the progress of pain, excessive hematuria or infection. Formation of stone, tuberculosis and tumors occasionally occur in association with polycystic disease of the kidney. Perinephric abscess, having its origin in infected cysts, at times requires drainage. Nephrectomy may be necessary, either to abolish the condition present or to prevent a general infection of the urinary tract. Surprisingly enough, patients with polycystic renal disease undergo the removal of a kidney well, especially those in the second or third decade of life. Apparently at this time there is a certain amount of regeneration of the remaining renal tissue. Walters and Braasch¹⁹ reported thirty-one cases in which nephrectomy had been performed; only one patient died, a man aged 67 who had adenocarcinoma of the kidney. Palliative surgical measures, such as incision and drainage of some of the larger cysts, are also in order in certain cases. Evidence of marked disturbance in function of both kidneys usually contraindicates surgical treatment except as an emergency method.

The chief cause of the destruction of the kidney is pressure atrophy of the parenchyma due to expansion of the cyst. There is marked atrophy of the parenchyma between and around the cysts, together with extensive areas of interstitial fibrosis. The majority of the glomeruli have undergone some hyaline changes, either complete or in patches, due to thickening of the capillary basement membranes.

HYPERPARATHYROIDISM

Hyperparathyroidism, represented either by parathyroid hyperplasia or by definite adenomas of one or more of the parathyroid glands, has long been known to affect the skeletal system and to produce decalcification, cysts, tumors and pathologic fractures of the long bones. More recently it has been shown that it may be the cause also of the formation of stones in the urinary tract and consequent renal insufficiency, together with an associated high value for nitrogen in the blood. The amount of calcium and phosphorus excreted in the urine is so greatly increased in this disease that not only are stones formed in the urinary tract but occasionally the deposits of calcium bodies and calcium infarcts so damage the kidneys that marked renal insufficiency develops. Barney and Mintz²⁰ stated that, as a rule in cases of hyperparathyroidism, formation of stone precedes the formation of lesions of bone, often by a period of several years. It is interesting to observe that in five of the twenty-nine cases reported by these observers there were skeletal lesions alone, while in thirteen the lesions were confined to the urinary tract and in eleven both skeletal lesions and lesions of the urinary tract were present.

Collip²¹ has shown that excessive doses of parathyroid extract administered to dogs resulted, in a few days, in death, which was preceded by anuria and retention of nitrogenous products. The dogs had calcium deposits in various organs, including the kidneys. Albright²² and his co-workers stated that an excessive

amount of the parathyroid hormone in the blood for a few days can so alter the equilibrium that calcium in some form is deposited in the tissues and death ensues. These authors stated that in certain cases of hyperparathyroidism the clinical picture is similar to that of chronic glomerulonephritis. The scarcity of casts in the urinary sediment is a helpful distinguishing point. They reviewed several cases. Hoffheinz²³ reported a case in which the clinical diagnosis included "contracted kidneys"; the concentration of nonprotein nitrogen in the blood was 221 mg. and the blood pressure was 85 systolic and 55 diastolic. The patient died in uremic coma. Necropsy revealed calcium bodies and calcium infarcts in the kidney. Besides a large coral-like stone which filled the upper part of the pelvis of the right kidney, there were many small stones in both kidneys. There were marked pyelonephritis and contraction of both kidneys. This case was of interest also in that all parathyroid glands showed formation of tumor.

In a case of McCallum's, reported by Albright, the patient had nausea, weakness and vomiting. Polyuria and nocturia were noted. The blood pressure was 140 and 100. The concentration of urea nitrogen was 185 mg. per hundred cubic centimeters of blood. The urine contained albumin and a few erythrocytes and leukocytes, and the specific gravity varied between 1.007 and 1.009. Both lower parathyroid glands were enlarged (2 by 1.5 cm.).

As to therapy for the prevention of renal damage associated with hyperparathyroidism, Albright²² pointed out that intake of fluids should be forced, that an alkaline reaction of the urine should be avoided, that administration of ammonium chloride and presumably other acidosis-producing salts is contraindicated, that a high phosphorus diet, while indicated for demineralization, imperils the kidneys and should be used only when the blood values can be followed carefully, and that the same rule applies to a high calcium diet, although to a less extent. He expressed the point of view that in almost all cases of this disease damage to the kidney eventually develops unless the condition is corrected by successful surgical measures.

WATER INTOXICATION

Water intoxication must be considered in the contemplation of nephritis and obstruction of the urinary tract. Water intoxication in itself causes symptoms of uremia, restlessness, asthenia, nausea, convulsions, coma and at times oliguria. If the main channel for the loss of water is closed by renal insufficiency or by obstruction of the urinary tract of any type, increasing the intake of fluids might cause a condition of water intoxication. The continued ingestion of water in an effort to cause diuresis and to reduce the concentration of nitrogen in the blood would only tend to increase the state of water intoxication.

On the other hand, surprisingly large amounts of water may be taken if the output is satisfactory. Rowntree²⁴ cited a patient of Trousseau's who had diabetes insipidus whose urinary output was 43 liters a day and whose intake of water was 40 liters. Even with the water exchange at this high level, signs of water intoxication did not appear, probably because of the prompt elimination of the water. Rowntree stated that in all probability it is not the quantity of water ingested

19. Walters, Waltman, and Braasch, W. F.: Surgical Aspects of Polycystic Kidney, *Tr. Am. A. Genito-Urin. Surgeons* 26: 385, 1933.

20. Barney, J. D., and Mintz, E. R.: The Relation of the Parathyroid Glands to Urinary Lithiasis, *Brit. J. Urol.* 8: 36-44 (March) 1936.

21. Collip, J. B., quoted by Albright, Baird, Cope and Bloomberg.²²

22. Albright, Fuller; Baird, P. C.; Cope, Oliver, and Bloomberg, Esther: Studies on the Physiology of the Parathyroid Glands: IV. Renal Complications of Hyperparathyroidism, *Am. J. M. Sc.* 187: 49-65 (Jan.) 1934.

23. Hoffheinz, S., quoted by Albright, Baird, Cope and Bloomberg.
24. Rowntree, L. G.: The Effects on Mammals of the Administration of Excessive Quantities of Water, *J. Pharmacol. & Exper. Therap.* 29: 135-159 (Oct.) 1926.

or the rate of exchange but rather an intake of an amount of water greater than the body can excrete that is responsible for the production of water intoxication.

Convulsions caused by water intoxication, when they occur, are general and of extreme potency and frequently resemble those due to strychnine poisoning. Water intoxication terminates in death unless the excessive intake is discontinued. A hypertonic solution of sodium chloride usually gives prompt relief from the symptoms. Rowntree, in his experimental work in an effort to obtain relief of symptoms, gave a hypertonic solution of sodium chloride to a group of dogs in various stages of water intoxication. Some of the dogs which were in a stupor, coma or convulsions improved strikingly within five to fifteen minutes after the administration of the solution; in fact, many of the animals appeared to be practically normal from a half hour to an hour later.

SUMMARY

Various urologic conditions markedly resemble, and not uncommonly lead to the diagnosis of, chronic glomerulonephritis. The most common conditions are infection, obstruction and certain metabolic disturbances. The majority of these diseases are readily recognized if a complete urologic examination is carried out. The similarity of these various urologic conditions to chronic glomerulonephritis leads to a diagnosis of nephritis. The fear that urologic instrumentation might be followed by serious reactions frequently prevents a complete study that would indicate the true nature of the lesion. In truth such fears are in most cases not warranted, as reactions rarely follow cystoscopy, with the present rapid, accurate methods, and the use of recently devised innocuous urographic materials. Carefully and gently carried out, such examinations cause no trouble even in patients with extremely damaged kidneys.

In all cases wherein there is even the slightest doubt as to the diagnosis, the patient should be given the benefit of a complete urologic investigation. If this is thoroughly carried out, a small but definite group of patients whose condition has been diagnosed as chronic glomerulonephritis will be found to have conditions that can be partially or completely relieved.

CONCLUSION

When a physician makes a diagnosis of chronic glomerulonephritis, he should be certain that the kidney itself is the seat of the disease and that the patient is not suffering from a curable condition simulating chronic glomerulonephritis.

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Medicine in the Third and Fourth Centuries.—Art, literature and medical knowledge all were slipping steadily backward in this third century. The soldiers in some of the far away provinces set up governments of their own, took barbarian wives, and were ready to resist compulsion from home. Zenobia, in her oasis at Palmyra, defied the Roman legions for years, for "she knew all science, history and military art"; but she was finally conquered and taken to Rome in A. D. 273, to complete the triumph of Aurelian. Her daughter became his queen, and in the next generation Zenobia's grand-daughter became queen of all Persia. She introduced Greek medicine into her medical school founded at Edessa. Indirectly, this helped to save Greek medicine to the world, for the successor of this school at Edessa became the great school of the fifth century at Gondashapur, with its medical library, its famous teachers and its Arab writers.—Hurd-Mead, Kate Campbell: *A History of Women in Medicine*, Haddam, Conn., the Haddam Press, 1938.

CHRONIC STREPTOCOCCIC ULCER OF THE SKIN

UNRESPONSIVE TO LOCAL THERAPY BUT CURED
BY SULFANILAMIDE: REPORT OF
TWO CASES

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BALTIMORE

Reports of chronic ulcerations of the skin in which the streptococcus plays a primary etiologic role cannot be found in the literature. Fissure and intertrigo with their occasional concomitants chronic recurrent erysipelas and lymphangitis, as Barber¹ pointed out, have been viewed heretofore as the most chronic lesions produced by this organism. The dermatoses of streptococcus origin are mostly acute or subacute and superficial. Even in ecthyma, as Sabouraud² emphasized, ulceration in the true sense does not occur, and as in other streptococcic pustular dermatoses the organism is simply present in the purulent exudate and ceases to act when free drainage and cleanliness by locally applied antiseptics are brought about and maintained for a shorter or longer period.



Fig. 1 (case 1).—Large ulcer on right forearm before treatment with sulfanilamide. The glazed appearance is due to the characteristic unpermeating serous exudate.

The type of ulcer which forms the basis for this report is apparently unique in that it was produced by streptococci, presented features of chronicity both clinically and histologically and occurred on the skin of healthy individuals. There is no previously recorded instance of an ulcer presenting the peculiar characteristics found in these cases, and the striking response to sulfanilamide of this type of lesion has also heretofore not been reported.

CASE 1.—History.—L. B., a white youth, aged 19, slender but in robust health, was seen Aug. 12, 1937, for a sore on the anterior surface of the right forearm and a smaller one on the anterior aspect of the right leg at the junction of the middle and lower thirds. There was nothing in the family or personal history relevant to the present illness. The patient stated that in the last week of June 1937 he had sustained insect bites to the arms and legs while in his home. All the bites disappeared with the exception of the ones from which the ulcers developed. These two areas became swollen and were quite red, painful and tender. July 1 he consulted a

Dr. J. Howard Brown gave advice in the bacteriologic studies.
From the Department of Dermatology, Johns Hopkins University
School of Medicine.

1. Barber, H. W.: *Prognosis in Streptococcal Infections of the Skin*, *Lancet* 2:35 (July 6) 1935.

2. Sabouraud, Raymond: *Ecthyma*, in *La pratique dermatologique* (Ernest Besnier, L. Brocq, L. Jacquet), Paris, Masson et Cie, 1:923-945, 1900.

physician, who incised the swelling on the right forearm and also that on the leg. In both areas open sores developed which did not yield to treatment with various antiseptics, including gentian violet and mercurial applications. The patient stated that a few days after the onset of the lesion on the forearm he noticed slight pain in the right armpit but that there was no diffuse redness or streaks of redness on the arm above the sore at any time. The pain in the armpit vanished in a few

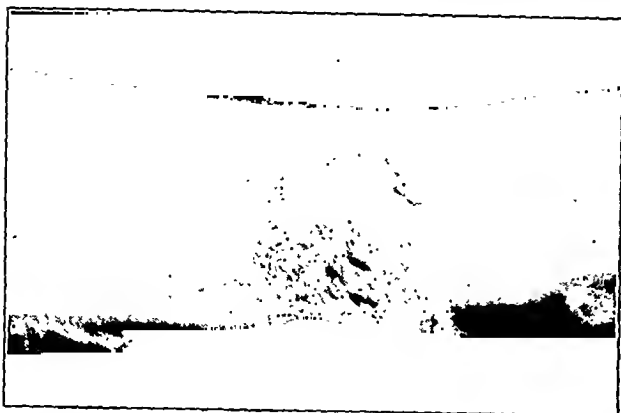


Fig. 2 (case 1).—The result (complete healing) obtained with sulfanilamide on the ulcer shown in figure 1.

days and he had had none since. The lesions became progressively larger and presented a rather curious aspect when first seen by me.

The lesion (fig. 1) on the forearm consisted of an ulcer, roughly oval, 2 by 3 inches (5 by 7.5 cm.) in diameter. The border was irregularly elevated throughout and was separated from the underlying tissues in such a manner that there resulted a marked undermining, at some places to a maximum distance of one-half inch (1.3 cm.). The skin of this uplifted border was ragged, frayed and serrated and with its bright red to dull red halo and induration presented a rather angry appearance. The redness extended in some areas, especially at the upper margin, to a distance of about 1 inch beyond the border, and within this zone there was marked tenderness on pressure. The depth of the ulcer varied from one-fourth to one-half inch (0.6 to 1.3 cm.), and the base presented smooth, grayish red, glazed, flattened, papilliform excrescences which were covered with a thin whitish yellow seropurulent exudate which could be easily wiped away. If wiping was carried out a little too energetically, there would result free bleeding from the granulations. On pressure over the margin of the ulcer a seropurulent fluid could be expressed. The lesion on the leg consisted of an ulcer which was circumscribed and rounded and measured 1 inch in diameter. It presented features similar to those of the lesion on the forearm except that there was less undermining and less redness about the border. This ulcer also discharged a thin seropurulent fluid.

The general physical examination disclosed no positive manifestations. The blood count showed red blood cells 4,710,000, white blood cells 10,100, with a differential percentage of polymorphonuclears 64, basophils 2, small lymphocytes 30, large lymphocytes 2 and transitionals 2. The Wassermann reaction of the blood was negative and an examination of the urine was negative.

Routine Treatment.—In spite of dressings alternately with 3 per cent aqueous-alcoholic gentian violet, a proprietary oxyquinoline benzoate compound ointment, 10 per cent ammoniated mercury ointment and boric acid ointment (U. S. P.), some fresh necrosis appeared in the margin of the ulcer on the forearm and in the adjacent normal skin. Thereafter a regimen of fomentations including warm compresses of 1:1,000 solution of mercury bichloride, 1:3,000 and 1:1,000 solution of potassium permanganate and solution of chloramine-T, 1 per cent, totaling six hours daily supplemented by cleansings with mild soap solutions and interval dressings with 2 per cent ointment of allantoin, ammoniated mercury, boric acid or 3 per cent

gentian violet effected no change over a period of several weeks. During this period a specimen was taken for biopsy from the inner border of the ulcer on the forearm.

Throughout the period of observation the patient occupied himself only with the treatment and spent a good deal of time at complete rest. During a short period of suspended treatment, bacteriologic studies were undertaken.

Laboratory Studies.—Smears made from the serous exudate showed a few gram-positive cocci in chains. Cultures were made on plain agar, beef broth, Loeffler's mixture, blood agar plates (surface inoculation) and desoxycholate agar plates. After forty-eight hours a single type of growth appeared on each of the mediums, with the exception of the desoxycholate agar medium,³ which inhibits the growth of streptococci; this was sterile. All the other mediums showed a pure growth of one and the same organism, which by deep inoculations into blood agar proved to be a beta hemolytic streptococcus. The blood agar surface showed a pure growth of a hemolytic streptococcus. The discovery in the stained smears (fig. 3) from the broth cultures of a tendency for the cocci to be arranged mostly in chains (at least more than six) with only occasional diplococoid formation would, in view of the source of the organism (from a seropurulent and nonerysipelatos lesion) and its manner of growth in bouillon, warrant designating it as *Streptococcus pyogenes longus* by the essentially morphologic classification proposed by von Lingelsheim⁴ in 1891. In spite of the fact that in the light of more recent bacteriologic work the division by von Lingelsheim of *Streptococcus pyogenes* into the group "longus," which is pathogenic, and the group "brevis" (in chains of six or less), which is nonpathogenic, has been proved to be totally arbitrary and unsupported by the facts, the name still persists to the present day in various textbooks to designate the common pyogenic streptococcus of the skin. Brown⁵ clearly showed that the grounds for such a division and labeling are untenable. In the same report he proposed his classification of the streptococci on the basis of their behavior in blood agar and their sugar-fermenting characteristics.

The beta hemolytic streptococcus cultured from the lesions in this case fermented lactose, salicin and trehalose but not mannite, inulin and sorbitol. It was thereby demonstrated to be *Streptococcus pyogenes* of human strain (as opposed to animal

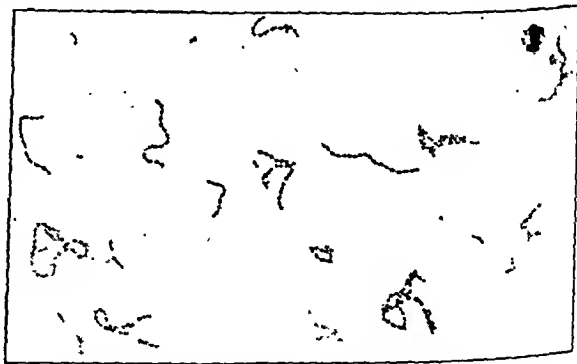


Fig. 3 (case 1).—Streptococci in smear from bouillon culture of exudate from ulcers. This *Streptococcus pyogenes* is still erroneously referred to as *Streptococcus pyogenes longus* because from bouillon culture it appears mostly in chains of at least six or more organisms.

strain).⁶ Judging from its behavior in the tissues, it is of low grade virulence, since it produced no lymphangitis and only a mild transient lymphadenitis.

3. Leifson, Einar: New Culture Media Based on Sodium Desoxycholate for the Isolation of Intestinal Pathogens and for the Enumeration of Colon Bacilli in Milk and Water, *J. Path. & Bact.* 40: 531 (May) 1935.

4. von Lingelsheim, H. A.: Experimentelle Untersuchungen über morphologische, kulturelle und pathogene Eigenschaften verschiedener Streptokokken, *Ztschr. f. Hyg. u. Infektionskr.* 10: 351-366, 1891.

5. Brown, J. H.: The Use of Blood Agar for the Study of Streptococci, Monograph 9, Rockefeller Institute for Medical Research, 1919, p. 87.

6. Edwards, P. R.: Further Studies on the Differentiation of Human and Animal Strains of Hemolytic Streptococci, *J. Bact.* 25: 527-536 (May) 1933.

Sections were prepared with hematoxylin and eosin stain, Verhoeff's elastic tissue stain and the bacterial stain of Brown and Brenn.⁷ There was a marked hyperplasia of the epidermis, most advanced at the edge that constituted the border of the ulcer, decreasing gradually from this point beyond toward the normal skin. In this pseudo-epitheliomatous border the prickly cells for the most part were swollen, unshapely, opaque and

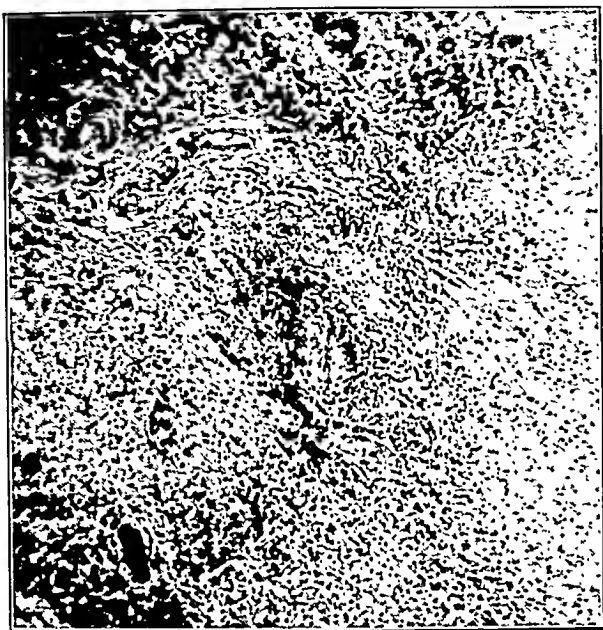


Fig. 4 (case 1).—Section from the edge of the large ulcer on the forearm. The infiltrate is of the chronic fixed tissue cell type with a preponderance of plasma cells and many lymphocytes and large mononuclears.

edematous and their nuclei were shrunken and pyknotic. The papillary bodies were extremely edematous, containing a fibrinous meshwork enclosing a loose infiltrate of lymphoid cells principally, some plasma cells, a few polymorphonuclear leukocytes and an occasional eosinophilic leukocyte. In the cutis proper the lymphatics were widely dilated and filled with a coagulum of serum, and down to the fatty layer the collagenous tissue, elastic tissue and blood vessels had suffered extensive degeneration and displacement by inflammatory cells which just back of the edge of the ulcer consisted of an abundance of polymorphonuclear leukocytes, many degenerated, but beyond this and throughout the section elsewhere of solid focal collections of plasma cells. In places, especially about remains of hair follicles and sweat glands, there was a solid infiltrate almost entirely of plasma cells. Many large mononuclear cells and a few eosinophils were found. However, here and there were seen some fibrin and free blood pigment. Back of the zone of intense inflammation there were a few dilated blood vessels surrounded by mantles of lymphocytes and plasma cells. The inflammatory process, therefore, consisted of a chronic fixed tissue cell type (fig. 4). At some distance beyond the edge of the ulcer and enclosed for the most part within the confines of these monocyctic cells there were revealed by the bacterial stain numerous cocci within phagocytic granulocytes and grouped in pairs and short chains lying free between the cells (fig. 5).

Course of Disease Under Sulfanilamide.—September 29, within forty-eight hours after the institution of sulfanilamide, the ulcers showed a sharp change. The remarkable healing effect on the lesions is outlined in table 1, which is self explanatory. The smaller ulcer was completely healed at least ten days before the larger one. The completely healed large ulcer with smooth, firm scar is illustrated in figure 2.

7. Brown, J. H., and Brenn, Lena: A Method for the Differential Staining of Gram-Positive and Gram-Negative Bacteria in Tissue Sections, *Bull. Johns Hopkins Hosp.* 48: 69 (Feb.) 1931.

CASE 2.—History.—M. F., an unmarried man, aged 29, a Russian-born Jew, slightly undernourished but well developed and intelligent, admitted to the Johns Hopkins Dermatological Clinic Nov. 15, 1937, complained of ulcers on both legs. There had been no tuberculosis in the family and aside from the fact that his mother had a goiter the family history was unimportant. He had always been in good general health. In childhood he had uncomplicated mumps. Following an attack of tonsillitis in 1924 his tonsils and adenoids were removed. In 1926 a gland was removed from the left angle of the mandible. While he was in the hospital for this operation an ulcer developed on the right shin which healed after several months. In 1928 and 1932 a series of small ulcers appeared on both legs, in each instance healing after several months. The last attack was associated with open sores on both ears, which healed with scars.

The patient's habits were fairly regular and until the onset of his present illness he had been employed as a salesman for a wholesale stationery store, which required that he be on his feet continuously eight hours a day.

The present illness began in the first week of June 1937, when a "red bump" appeared almost simultaneously on the lower third of each leg. These areas broke down into open sores, which gradually enlarged into discharging ulcers within about three weeks. At this time he came under competent medical management, but in spite of routine general measures and continuous local treatment of the ulcers, including the application of fractional x-rays, ultraviolet rays, various antiseptic fomentations, stimulating agents such as tar oils, and protective and antiseptic ointments, the lesions slowly increased in size until his admission to the Johns Hopkins Dermatological Clinic. His physician personally communicated his opinion that the ulcers were probably tuberculous. At no time in the course of the disease had there been lymphangitis or femoral or inguinal lymphadenitis to an appreciable degree.

Examination.—The general physical examination was negative except for the presence of a deflected nasal septum and posterior nasal discharge. A roentgenogram of the chest was negative.

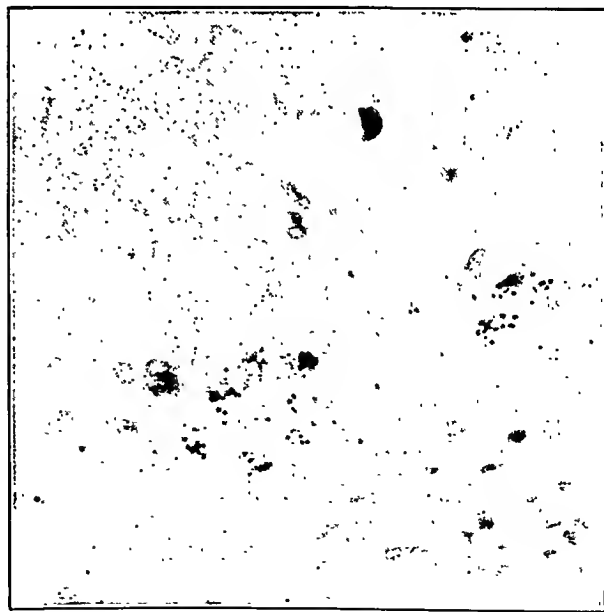


Fig. 5 (case 1).—Section shown in figure 5, stained with Brown and Brenn's bacterial stain. Numerous cocci within phagocytic granulocytes and grouped in pairs and short chains between the inflammatory fixed tissue cells.

In general the skin and accessible mucous membranes were of good texture and color. There were a few tiny depressed scars in the margins of the ear lobes. In the anterior triangle of the neck on the left side was an irregular elongated hypertrophic scar. Over both legs there were a number of superficial

scars varying in size up to a half dollar (30 mm.). There was a moderate cyanotic tint of the legs when dependent, and numerous superficial varicosities were present. The dorsalis pedis artery was barely felt in each extremity.

Rather symmetrically occupying the inner aspect of the lower third of each leg and extending down slightly to the anterior and posterior surfaces was a large roughly circular ulcer about the size of the palm (fig. 6). The border was mostly serpiginous but at a few points its outline was jagged, dentate or angulated. The base was very uneven and presented in places glazed rough granulations which protruded to the level of the border but in other areas formed depressions or gullies which reached a depth from the surface of the skin of as much as 2 cm. The entire edge of the border was inflamed, but in some zones it was only slightly so, smooth, thin and well attached to the base, whereas in others it was thickened and infiltrated, quite angrily red, rough, necrotic looking and undermined. This infiltration and redness extended in places to a distance of 1 cm. beyond the edge. The base of the ulcer was covered with a copious yellowish thin seropurulent exudate, which one could express from the undermined portions by pressing on the overlying skin. Slight pressure over the border or base of the ulcer elicited tenderness, but there was no spontaneous pain. On each leg just above the large ulcer there was a superficial one, the size of a half dollar, exuding a copious serous fluid. The patient stated that these ulcers had appeared in the last few weeks. There was no enlargement or tenderness of the femoral or inguinal lymph glands.

Laboratory Studies.—At the time of admission the Wassermann reaction of the blood was negative and examination of the urine was negative. The blood count showed red blood cells

tory process of the same nature as that found in case 1, but the chronic features were exaggerated in that the plasma cell and lymphoid cell infiltrate was accompanied by numerous discrete and solidly grouped large mononuclear cells to such a degree that a competent dermatopathologist who also saw the patient felt very strongly that the condition might be tuberculous.

Course of Disease Under Sulfanilamide.—After the patient received three 20 grain (1.3 Gm.) doses of sulfanilamide daily

TABLE 2.—*Series (Continuous) of Treatments with Sulfanilamide in Case 2*

Daily Ingestion of Sulfanilamide from Nov. 16, 1937, to Feb. 8, 1938 Total Daily Dosage			
Divided into Three Equal Doses		Divided into Four Equal Doses	
1937	Grains	1937-1938	Grains
November 16-19.....	60	November 28-30.....	60
November 20-23.....	45	December 1-13.....	60
November 24-27.....	30	December 14-15.....	60
		December 16-21.....	60
		December 22-28.....	60
		December 29-January 8.....	100
		January 9-11.....	60
		January 12-15.....	60
		January 16-22.....	40
		January 22-February 8.....	90

After three days of treatment, heelrag commenced in all the ulcers; it is probable that by Nov. 27, 1937 (see text) only minimal doses were necessary because the progressive heelrag was influenced by the increased doses which were given from Nov. 28, 1937, to the date of complete healing of the large ulcers on Feb. 8, 1938

TABLE 1.—*Effect of Sulfanilamide on the Ulcers in Case 1*

Total Daily Quantity of Sulfanilamide Taken as Three Equal Separate Doses (Treatment Began Sept. 27, 1937)		
Date	Grains	Comment (Large Ulcer on Right Forearm)
September 27.....	60	Markedly undermined unhealthy border with copious yellow discharge
28.....	60	
29.....	60	Ulcer dry and covered with healthy crust—groove of undermining obliterated
30.....	45	
October 1-2.....	45	
3-5.....	30	
6.....	15	
7.....	15	Reappearance of undermining at three points with copious discharge
8-10.....	60	
11.....	60	Lesion dry and healthy—again groove of undermining obliterated
12.....	60	
13.....	45	Smooth fresh seal of healing advancing from border
14-16.....	45	
17.....	45	At least 5/6 of ulcer closed with smooth seal—small central dry crust remaining
18-20.....	30	
21.....	30	Entire ulcer healed except for pen-sized area in center
22.....	30	
23-31.....	15	
November 1-2.....	15	
3.....	15	Complete healing with smooth seal

The small ulcer on the right leg completely mimicked in appearance and course the large ulcer before and during the administration of sulfanilamide. The former was completely healed October 25.

5,120,000, hemoglobin content 100 per cent, white blood cells 9,900, with a differential of juvenile neutrophils 2 per cent, segmented neutrophils 68 per cent, basophils 2 per cent, lymphocytes 19 per cent and monocytes 9 per cent. The tuberculin test was strongly positive to 0.001 mg. and 0.01 mg. of tuberculin.

The bacteriologic result was the same as that in case 1, with the minor exception that the streptococcus in this instance fermented trehalose more slowly.

Microscopic study of a biopsy specimen obtained from the border of the large ulcer on the left leg revealed an inflamma-

tion for three days (a total of 180 grains or 12 Gm.) the undermining in the borders in most areas was obliterated, the discharge was free from pus and consisted of a thin, straw-colored serous fluid, and its quantity was definitely reduced. The borders of the ulcers also appeared thinner, lost their necrotic appearance in most places and looked healthier. Treatment with the drug is outlined in table 2. After the third day of treatment healing set in at the borders of the ulcers and progressed slowly but surely. To note the effect of increased dosage, the patient, November 28, began to ingest a daily total dosage of 60 grains (4 Gm.) divided into three 5 grain (0.3 Gm.) tablets four times a day. The various levels of dosage by this schedule, as noted in table 2, were maintained for unusually prolonged periods. The only changes that occurred in the ulcers consisted of a further diminution in the quantity of discharge, but healing at the margins progressed at the same pace as previously. The small ulcers healed within two weeks from the commencement of sulfanilamide therapy. By December 30 the large ulcers were reduced to something less than half their original size. The patient appeared in excellent physical condition, having gained 12 pounds (5.4 Kg.). Aside from a slight nausea for a few days after the institution of sulfanilamide therapy, which was overcome by sodium bicarbonate taken only for a short period, he exhibited no cyanosis or other toxic effect. On this date examination of the blood for methemoglobin was negative, and the cell count showed red blood cells 5,300,000, hemoglobin content 97 per cent, white blood cells 5,700, with a differential percentage of segmented neutrophils 64, basophils 1, lymphocytes 28, and monocytes 7.

Throughout the period of sulfanilamide therapy local treatment for the ulcers consisted only of simple boric acid ointment dressings, changed every four days. Beginning Jan. 4, 1938, the use of gentian violet 2 per cent aqueous solution and oil of cadeberry on the ulcer of the left leg failed to produce any appreciable difference in the rate of healing of the two ulcers.

At this time it was felt advisable to see whether any special benefit would accrue by raising the intake of sulfanilamide to at least the maximum standard dosage originally advocated by Long and Bliss⁸ for severe infections in order to attain

8. Long, P. H., and Bliss, Eleanor A.: The Use of Para-Amino-Benzenesulfonamide (Sulfanilamide) or Its Derivatives in the Treatment of Infections Due to Beta Hemolytic Streptococci, Pneumococci and Meningococci, South. M. J. 30: 479-487 (May) 1937.

quickly a blood level of 10 mg. per hundred cubic centimeters. Beginning January 9, such increase in dosage was made but no added benefit resulted. By January 18 the ulcers were reduced to the size of a half dollar. Culture mediums of the same type as those originally used were inoculated with the serous exudate of each ulcer. Within twenty-four hours all the mediums were overgrown with *Staphylococcus albus*; there was not a single colony of streptococci. The ulcers were completely healed on February 8 (fig. 7).

COMMENT

In each of two cases there was introduced into the skin a variety of beta hemolytic streptococcus capable of producing a low grade necrosis leading to chronic ulceration. The organism proved to be a *Streptococcus pyogenes* of human strain. When accidentally transferred to the normal skin, it produced an area of redness and edema which softened and became necrotic. The resulting ulcer was superficial and when treated early with locally applied antiseptics healed quite rapidly. However, if not interfered with the streptococcus apparently invades deeply to produce undermining with slowly progressive extension of the ulcer. In both cases the ulcers had enlarged with an irregular, firm, thickened, angrily red, ragged, undermined border and uneven deepening of a roughly granular glazed base, discharging continuously a copious serous fluid. Other than a slight and transient regional lymphadenitis, there were no complications. The biopsy studies revealed the presence of intracellular and extracellular cocci in pairs and short chains, and in various types of mediums inoculated with exudate from the ulcers a pure culture of the streptococcus was obtained. This fact is of particular interest because, as Barber¹ has so emphatically stated in his discussion of streptococcic infections of the skin, streptococcic lesions always become secondarily infected with staphylococci, whereas staphylococcic lesions usually remain pure.



Fig. 6 (case 2).—Large ulcer on left leg, showing undermined border and uneven base covered with serous exudate.

In case 1 it was totally impossible to effect healing by means of local antiseptic treatment. This was unquestionably due to the fact that the organisms, enclosed in a chronic fixed tissue cellular infiltrate in the region of the undermined portion of the ulcers, were beyond the reach of the agents applied. The sharp and prompt effect of sulfanilamide on the ulcers in case 1 not only solved the problem of therapy but gave confirmatory evidence that the ulcers were of primary streptococcus (beta hemolytic) etiology.

The ulcers of the leg in case 2 were each about four times the size of the large ulcer of the right forearm in case 1. The effect of sulfanilamide on these ulcers was as sharp and prompt as in case 1. The dosage of the drug used at the commencement of treatment in case 2 was based on the experience with case 1, and it can be safely assumed that sterilization of the lesions took place as a result of the initial "course" of sulfanilamide, ranging from a total daily dosage of 60 grains to the gradually reduced dose of three 5 grain tablets

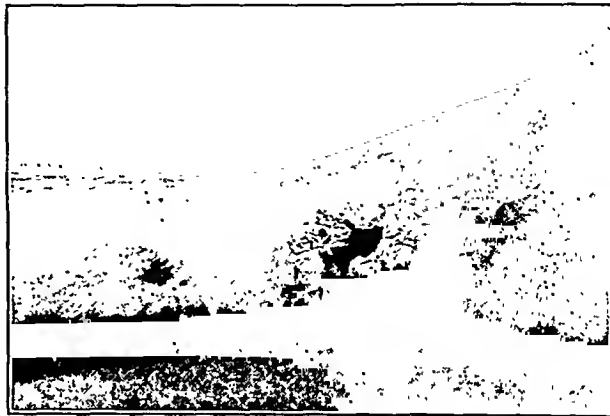


Fig. 7 (case 2).—The result (complete healing) obtained with sulfanilamide on the ulcer shown in figure 6. Note the residual scalliness over the small freshly healed area.

a day (table 2). The slower healing in case 2 as compared to that in case 1 was obviously due to the larger size of the ulcers in the former case and to their location on the lower extremities, and the presence of numerous varicose veins in that case.

CONCLUSIONS

1. The complete records of two cases of a hitherto unreported type of primary ulcer of the skin produced by a beta hemolytic streptococcus are added to the literature on streptococcic infections.
2. This type of ulcer is characterized by its pronounced chronicity and extreme resistance to local treatment.
3. Clinically the ulcer presents a markedly inflamed, slowly necrosing, undermined, mostly serpiginous border with a deep uneven and glazed, roughly granular base discharging continuously a copious thin yellowish serous fluid.
4. Histologically the ulcer presents a chronic fixed tissue cellular reaction.
5. Prompt cure of the ulcers in the two cases was brought about by sulfanilamide, which exercised a strikingly specific effect.

NOTE.—Since completion of this article a third case has been observed. A white woman, aged 23, in excellent general health by hospital survey, complained of a group of five large confluent ulcers on the left leg and three on the right leg which failed to respond to continuous medical management with intensive local treatment for several months. These lesions proved to be essentially identical to those reported clinically, histologically, bacteriologically and in their response to sulfanilamide. Also a fourth case of similar type was observed, which, because of unavoidable circumstances, could not be followed with respect to sulfanilamide therapy.

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RECENT STUDIES ON EXPERIMENTAL
LOBAR PNEUMONIA

PATHOGENESIS, RECOVERY AND IMMUNITY

O. H. ROBERTSON, M.D.

CHICAGO

I. PATHOGENESIS

Very little is known concerning the optimum conditions for the inception of lobar pneumonia in the human being. That some disturbance in pulmonary function precedes the onset of this disease in the majority of cases seems probable in view of the frequency of antecedent acute infection of the upper part of the respiratory tract, but the manner in which such infection lowers the resistance of the lung to invasion by pneumococci can only be conjectured. Furthermore, in a considerable number of instances lobar pneumonia occurs during a period of apparent good health. An experimental approach to this problem has been carried on in several ways. My associates and I sought to determine first whether or not variations in individual resistance to the different types and strains of pneumococci might be related to the inception of infection. An earlier study of the pneumococcus-killing activity of the blood of various animals revealed the presence of marked species differences in the exhibition of this property. The blood of pneumococcus-resistant animals was found to be capable of killing great numbers of pneumococci, while that of susceptible species either lacked pneumococcidal power or showed it to only a slight degree.¹ This action of the blood was found to depend entirely on the opsonic content of the serum. Leukocytes of susceptible animals were just as active as those of resistant ones in the presence of a potent opsonic serum.²

While the pneumococcidal action of the blood (serum and leukocyte mixtures) did not represent the entire mechanism of natural immunity to the pneumococcus, it did provide a means for determining the factor of humoral immunity in the human being. Tests on the blood of a group of normal persons showed that there exist fully as marked individual variations in respect to the pneumococcus-killing power as were found between the different animal species.³ This observation suggested the possibility that persons contracting pneumonia might belong to the group without demonstrable pneumococcidal action in the blood. Accordingly observations were made on the blood of patients with pneumonia early in the course of the disease, in certain instances from four to six hours after the onset of the illness. The tests showed great divarication. Some of the patients were found to possess no blood-killing power for the pneumococcus causing the infection, while

others exhibited this property to a normal degree. We have no proof that the normal pneumococcus-killing activity was present in the same degree immediately before infection, yet repeated observations on normal persons and on patients suffering from various types of infection of the respiratory tract (studied by Graeser and Harrison⁴) have shown that this characteristic of the blood does not fluctuate rapidly. Hence it seems fair to assume that lobar pneumonia can occur in the presence of a normal pneumococcidal activity of the blood, and this suggests that the inception of the pneumonic infection depends more on some local change in the lung than on fluctuations in general antipneumococcic resistance.

These observations lead to a more detailed consideration of the pathway by which pneumococci gain entrance to the lung. There can be little doubt in view of the accumulated evidence, both clinical and experimental, that the pneumococci producing pneumonia are implanted in the lung by way of the air passages, and that particulate matter may be carried to the terminal air sacs can be inferred from the finding of carbon and other particles in the alveolar macrophages. Also it is known that the lung possesses a remarkably efficient mechanism for the elimination of inhaled material. This consists of the ciliary activity of the bronchial mucosa, the alternate expansion and contraction of the bronchi with each respiration, together with a possible peristaltic contraction of the air tubes, and the cough reflex. Thus foreign material taken into the bronchi is fairly easily eliminated, but if it enters the alveoli expulsion is much more difficult, since neither the alveoli nor the ducts leading to them are provided with cilia or musculature and the bottle-like shape of the terminal air sac offers additional obstruction to egress. However, the alveolar macrophages present in small numbers in the normal lung are capable of disposing of most kinds of inspired substances. Under normal conditions the clearing functions of the lungs are so efficient that the lower part of the respiratory tract is kept practically sterile.

Is there any evidence that interference with the normal eliminatory mechanism of the lung has an important role in the inception of lobar pneumonia, and what effect may the so-called predisposing factors exert in this respect? While some of these factors, such as the inhalation of irritating and poisonous gases and of anesthetics, partial drowning and the inspiration of various sorts of material during operation, in all probability produce a disturbance of the lung's clearing function, pneumonias following such disturbances constitute a relatively small proportion of cases of this disease. The one condition which precedes pneumonia in the great majority of cases is the common cold.⁵ What action a cold may have on the eliminatory mechanism of the lung can only be surmised, although in certain cases in which the infection has reached the lower part of the respiratory tract local obstruction of the smaller air passages may well occur. However, the effect of chilling of the body surface during a cold does seem to have a more direct relationship to the

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These studies represent the combined collaboration of a number of investigators, including R. H. P. Sia, J. B. Graeser, E. E. Terrell, L. T. Coggeshall, C. G. Loosli, C. G. Uhley, John Fox, Morton Hamburger, H. M. Van Sant and M. A. Cornwell.

1. Robertson, O. H., and Sia, R. H. P.: Studies on Pneumococcus Growth Inhibition: II. A Method for Demonstrating the Growth-Inhibitory and Bactericidal Action of Normal Serum-Leucocyte Mixtures, *J. Exper. Med.* 59: 219-244 (Feb.) 1924.

2. Robertson, O. H., and Sia, R. H. P.: Studies on Pneumococcus Growth Inhibition: VII. The Relation of Opsonins to Natural Resistance Against Pneumococcus Infection, *J. Exper. Med.* 46: 239-262 (Aug.) 1927.

3. Robertson, O. H., and Cornwell, M. A.: A Study of the Resistance of Normal Human Beings to Recently Isolated Strains of Pathogenic Pneumococci, *J. Exper. Med.* 52: 267-277 (Aug.) 1930.

4. Robertson, O. H.; Terrell E. E.; Graeser, J. B., and Cornwell, M. A.: The Relation of Natural Humoral Antipneumococcal Immunity to the Inception of Lobar Pneumonia, *J. Exper. Med.* 52: 421-433 (Sept.) 1930.

5. Graeser, J. B., and Harrison, M. C.: Changes in the Titer of Antipneumococcal Humoral Immunity in Adult Human Beings, *J. Exper. Med.* 58: 245-252 (Aug.) 1933.

6. The striking predisposing factor of epidemic influenza may be similar to that of the cold but not unlikely represents a general irritative or injury of the respiratory tract.

onset of pneumonia, since many patients give a history of such an occurrence immediately before the inception of the disease. Here again the nature of the disturbance caused by chilling is not altogether clear. Certain effects on the mucosa of the upper part of the respiratory tract, such as a fall in surface temperature and vasoconstriction, have been observed by Mudd and his co-workers⁷ to accompany depression of the temperature of the skin in the human being. Nedzel⁸ has shown a similar lowering of the temperature of the respiratory mucosa as far down as the lower part of the trachea in experimentally chilled dogs.

PRODUCTION OF EXPERIMENTAL LOBAR PNEUMONIA IN THE DOG

Making use of the conception that local obstruction of the air passages and chilling create conditions suitable for the onset of pneumonia, we proceeded to devise a method for the production of experimental pneumonia in the dog, with doses of pneumococci somewhat comparable to those which might be supposed to cause the disease in man. The dog seemed to be a suitable animal, since its blood exhibits about the same degree of pneumococcidal action as that of the average human being. Small quantities of pneumococcus culture of type I or II were suspended in a starch-broth medium of about the viscosity of sputum and injected through a radiopaque catheter inserted into a terminal bronchus with the dog under the fluoroscope. The animal had previously received a dose of morphine sufficient to lower the body temperature from 4 to 6 degrees F. The larynx was cocaineized to prevent coughing. In this manner it was possible to produce constantly a lobar pneumonia in the dog which closely resembled the disease which occurs spontaneously in man.⁹ The average course of the disease was three or four days. Recovery often occurred by crisis. When doses of less than 0.01 cc. of culture were employed the disease occasionally failed to develop, but well marked pneumonia resulted from as little as 0.00001 cc. of culture. With the smaller doses, from 0.001 to 0.02 cc., the pathologic process usually remained confined to a single lobe and the animal recovered. With larger doses, 0.05 to 0.1 cc. or more, spread from lobe to lobe took place and the mortality rose with the increasing size of the infecting inoculum. Bacteremia, leukopenia and extension of pulmonary involvement were found to have the same prognostic significance as in human beings.

EVOLUTION OF THE CANINE PULMONARY LESION

A study was then undertaken of the changes occurring in the pulmonary lesions from the time of their inception until recovery or death.¹⁰ The animals were killed at varying intervals by means of the rapid intravenous injection of pentobarbital sodium. Within an hour after the implantation of the infecting dose of pneumococci at the periphery of the lung the micro-organisms were seen to be lying principally within the air sacs embedded in the starch, but already they were

observed to be migrating away from the focus of infection. One of the early reactions to the growth of the pneumococci in the lungs is the outpouring of edema fluid into the air spaces. This has been observed by Loeschke¹¹ in human beings with pneumonia and by Rhoads and Goodner¹² in rabbits with experimental dermal pneumococcal infection. While the exudation of edema is a protective mechanism on the part of the body, presumably an attempt to dilute the toxic substances elaborated by the growing pneumococci, it also has the effect of dispersing the micro-organisms in the tissues.

A recent study by Sutliff and Friedemann¹³ has shown that the pneumococcus during its growth produces a substance which when injected into the lungs or under the skin causes a local outpouring of edema such as occurs during pneumococcal infection. The pneumococci are probably spread through the lung to a certain extent by the lymph channels. However, they are

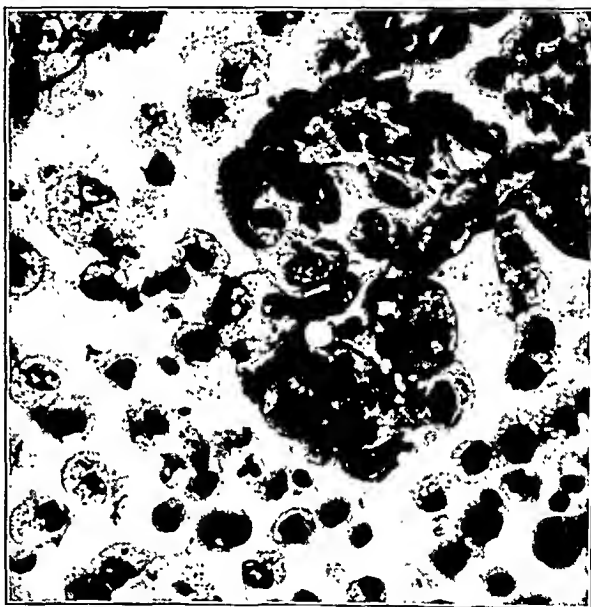


Fig. 1.—Section of lung of a dog killed just after recovery from experimental lobar pneumonia ($\times 625$). The greatly thickened alveolar wall contains many large mononuclear cells, which are becoming detached to form macrophages of the resolution exudate.

seldom seen in the alveolar walls after the first hour or two, and many of the micro-organisms which appear to be in the septal tissue are actually adhering to its surface, as can be shown by a technic devised by Loosli.¹⁴ Our observations would indicate that the pneumococci are carried chiefly in the infected edema fluid, which can pass along the air ways and also from air sac to air sac by means of small apertures in the walls, the pores of Cohn. Until the recent observations of Macklin¹⁵ and particularly the experimental work of Loosli¹⁴ there was much difference of opinion as to whether these communicating openings were artefacts or normal structures. Loosli has shown con-

7. Mudd, S.; Goldman, A., and Grant, S. B.: Reactions of the Nasal Cavity and Post-Nasal Space to Chilling of the Body Surface, *J. Exper. Med.* 34: 11-45 (July) 1921.

8. Nedzel, A. J.: Exposure to Cold as a Factor in the Etiology of Lobar Pneumonia, *Illinois M. J.* 68: 340-345 (Oct.) 1935.

9. Terrell, E. E.; Robertson, O. H., and Coggeshall, L. T.: Experimental Pneumococcus Lobar Pneumonia in the Dog: I. Method of Production and Course of the Disease, *J. Clin. Investigation* 12: 393-432 (March) 1933.

10. Robertson, O. H.; Coggeshall, L. T., and Terrell, E. E.: Experimental Pneumococcus Lobar Pneumonia in the Dog: III. Pathogenesis, *J. Clin. Investigation* 12: 467-493 (March) 1933.

11. Loeschke, H.: Untersuchungen über die Kruppöse Pneumonie, *Beitr. z. path. Anat. u. z. allg. Path.* 86: 201-223 (Jan. 3) 1931.

12. Rhoads, C. P., and Goodner, Kenneth: Pathology of Experimental Dermal Pneumococcus Infection in Rabbits, *J. Exper. Med.* 54: 41-50 (July) 1931.

13. Sutliff, W. D., and Friedemann, T. E.: A Soluble Edema-Producing Substance from the Pneumococcus, *J. Immunol.*, to be published.

14. Loosli, C. G.: Intervascular Communications in Normal and in Pathologic Mammalian Lungs, *Arch. Path.* 24: 743-776 (Dec.) 1937.

15. Macklin, C. C.: Alveolar Pores and Their Significance in Human Lung, *Arch. Path.* 21: 202-216 (Feb.) 1936.

clusively by means of ingenious experiments that they are normal structures. He has demonstrated in the lesions of experimental pneumonia bands of fibrin passing through pores with contained pneumococci.

Sections taken from the infected lung during the early stages of the experimental disease show that the inflammatory lesion spreads in a fairly regular fashion. Adjoining the normal tissue is an outermost zone of edema-filled air sacs containing many pneumococci. Following the outpouring of edema fluid is a migration of red blood cells and polymorphonuclear leukocytes into the alveoli, and the latter begin to phagocytize the micro-organisms. This constitutes a second zone nearer the central, or original, site of infection, where the concentration of leukocytes is greatest. Here the pneumococci are fewer in number and all within the cells where they undergo digestion. Since the process of phagocytosis takes time, an interval elapses between the arrival of the leukocytes and the ingestion of the

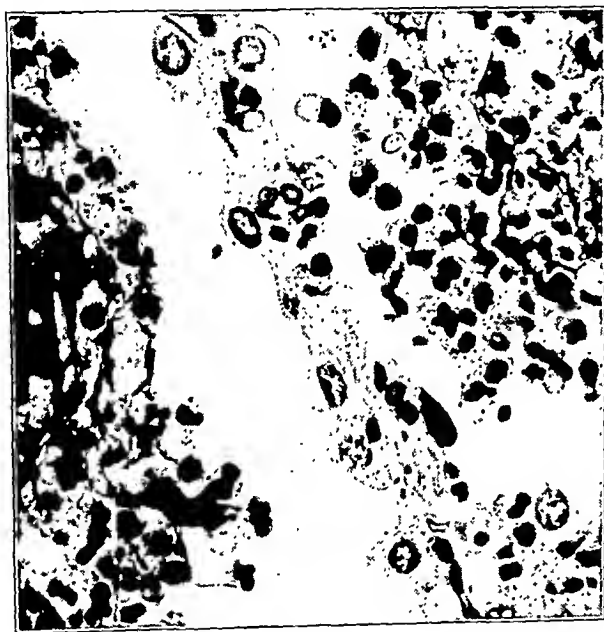


Fig. 2.—Section of consolidated lung from a person who had lobar pneumonia ($\times 700$), showing beginning macrophage reaction; the thickened alveolar wall contains numerous large mononuclear cells which protrude into air spaces. The intra-alveolar cellular exudate is still predominantly polymorphonuclear.

pneumococci. This permits the further peripheral spread of the infected edema fluid and affords an explanation of the problem as to how pneumonia can spread in the lung in the presence of a normal pneumococcus-killing power of the blood. If this is the correct interpretation of the mechanism of the extending lesion it should be possible by accelerating the process of phagocytosis and digestion locally to check the spread of the infection. This we have been able to do by injecting a high concentration of opsonins and leukocytes with the infecting dose of pneumococci. The lesions resulting from this procedure were very circumscribed and soon became sterile.¹⁶

The question then arose as to whether the successful production of lobar pneumonia by the method described depended principally on interference with the eliminatory function of the lung or on the implantation of the

pneumococci in the terminal air sacs. Earlier observations on dogs showed that the simple injection of small amounts of pneumococcus cultures even into the bronchi only occasionally resulted in infection, and this was of a mild nature.¹⁷ In an attempt to answer this question Hamburger¹⁸ has carried out a series of experiments in which suspensions of pneumococci were forcefully sprayed into the main bronchi of morphinized dogs. While this work is not yet completed the results in general suggest that obstruction of the terminal bronchi is the more important of the two factors.

Our finding that with experimental canine pneumonia the size of the infecting dose bears a direct relationship to the inception and outcome of the disease raises the question as to whether dosage may be an important factor in determining the development of lobar pneumonia in the human being. Suggesting this possibility are the observations of Webster and Hughes,¹⁹ who have shown that the numbers of pneumococci in the upper part of the respiratory tract often increase greatly during a cold, but other epidemiologists have not observed such a direct association. However, Smillie and Leeder²⁰ found a higher incidence of the more pathogenic pneumococci, types I and II, in pneumonia contacts with colds than in normal contacts.

II. RECOVERY

The changes observed in the pathogenesis of the pneumonic lesion in the dog are in every way analogous to those seen in the various stages of early primary and young metastatic processes observed post mortem in cases of human lobar pneumonia.²¹ The further development of both the canine and the human lesions proceeds in the same manner. At first the polymorphonuclear leukocytes are able to digest the pneumococci but later in the course of the disease they seem to lose this function, as numbers of normal appearing micro-organisms are visible within the cells and many are free in the younger parts of the inflammatory process. This is the usual picture just before recovery. With the onset of recovery a sudden change occurs, in which the pneumococci in the lungs are rapidly destroyed and the disease terminated. The only known means by which pneumococci are disposed of is phagocytosis and intracellular digestion. Hence it seems evident that in order to bring about a rapid termination of the infection the body must either develop a marked increase in the so-called natural antipneumococcal processes present before and often during infection or develop a new type of reaction. Supporting the latter alternative is the fact that in most cases of lobar pneumonia both in adults and in children the blood develops at about the time of recovery a much greater pneumococcus-killing power than it possessed formerly or is present in normal human beings. This property

17. This result is quite different from that obtained by Blake and Cecil, who produced lobar pneumonia in monkeys by the intratracheal injection of very small doses of pneumococcus culture (Blake, F. G., and Cecil, R. L.: Studies on Experimental Pneumonia: Production of Pneumococcus Lobar Pneumonia in Monkeys, *J. Exper. Med.* **51**: 403-444 [April 1920]).

18. This work is being carried on in the author's laboratory and is not yet reported.

19. Webster, L. T., and Hughes, T. P.: The Epidemiology of Pneumococcus Infection: The Incidence and Spread of Pneumococci in the Nasal Passages and Throats of Healthy Persons, *J. Exper. Med.* **53**: 535-552 (April) 1931.

20. Smillie, W. G., and Leeder, F. S.: Epidemiology of Lobar Pneumonia, *Am. J. Pub. Health* **21**: 129-138 (April) 1920.

21. The recent study of experimental pneumococcal lobar pneumonia in the rat by Gunn and Nungester indicates that the evolution of the murine and that of the canine lesions are also essentially the same (Gunn, F. D., and Nungester, W. S.: Pathogenesis and Histopathology of Experimental Pneumonia in Rats, *Arch. Path.* **21**: 813 [June] 1936).

16. Robertson, O. H.: The Effect of Increased Antipneumococcal Immunity on the Inception of Experimental Lobar Pneumonia in the Dog, *J. Exper. Med.* **66**: 705-727 (Dec.) 1937.

depends on the presence of acquired heat-stable opsonins. While these newly produced immune substances undoubtedly play a part in the process of recovery, it has not been possible to assign to them the primary role in this mechanism, since in some instances they are not detectable in the blood until several days after recovery or may appear two or three days before the end of the disease. In not more than half the cases does their occurrence in the blood coincide exactly with the onset of recovery.²² The best evidence for the effective action of such immune substances is the results obtained in the serum treatment of early pneumonia. However, if treatment with serum is begun after the disease is well advanced the infection in most instances persists until the usual time of recovery or death.

Our studies of the pneumonic lesions of dogs killed at the time of recovery have brought to light another mechanism which appears to play an important part in this process. At the beginning of recovery there occurs in the infected lung a striking histologic transformation. The alveolar walls become thickened, owing to the presence of large mononuclear cells, which first protrude into the air spaces and then become free and enter the exudate as actively phagocytizing cells, macrophages (fig. 1). They engulf the red cells, polymorphonuclear leukocytes and pneumococci, which they digest rapidly. Associated with their advent is solution of the fibrin, thinning of the intra-alveolar exudate and resolution of the lesion.²³

MACROPHAGE REACTION IN HUMAN LOBAR PNEUMONIA

The next step was to determine whether or not the cellular change which we have designated as the macrophage reaction occurred in the human lung at the time of recovery from pneumonia. This we were able to do only indirectly, by a study of the resolving areas in lungs examined post mortem. Microscopic examination of such tissues revealed the presence of a well marked macrophage reaction. Furthermore, the beginnings of this process were found in areas which were still intensely consolidated (fig. 2). The different stages resembled in every respect the changes observed in the dog.²⁴ Of great interest was the finding that wherever the mobilization of macrophages was marked the pneumococci were few or absent. Sometimes a single lobe in the state of resolution appeared to be entirely freed of pneumococci while a younger lesion showed micro-organisms in great numbers. The macrophages appeared to be capable of engulfing and digesting large numbers of pneumococci, but the polymorphonuclear leukocytes at this stage appeared to have lost their digestive activity. Whether this is the only method by which the body disposes of the invading micro-organisms we do not know. Curphey²⁵ has bridged the gap between our experimental observations and the postmortem studies by means of biopsies performed on the lungs of patients during the course of

lobar pneumonia. He showed that the cellular reactions which we have observed in the resolving lung after death occur during recovery.

PHAGOCYtic AND DIGESTIVE ACTIVITY OF MACROPHAGES VERSUS POLYMORPHONUCLEARS

We undertook a study of the phagocytic and digestive activity of macrophages, comparing them with polymorphonuclear leukocytes, both in the test tube and in vivo. Suspensions of macrophages were obtained by injecting acacia into the pleural cavity of dogs. The polymorphonuclear leukocytes were secured by similar injections of aleuronat. These cells were washed free from their native fluid and added to opsonic fluids of varying concentration containing pneumococci. The difference between these two types of cells with respect to their ability to phagocytize and digest pneumococci was striking. The macrophages took up the micro-organisms promptly and digested them so rapidly that sometimes within an hour or two all the pneumococci had melted away within the cells. On the other hand, the polymorphonuclears acted much more slowly, often taking many hours to accomplish the same result, and unless the concentration of opsonins was sufficiently high complete digestion did not occur. Identical results were obtained when pneumococci were injected into the chest cavities containing the two kinds of exudates and samples withdrawn for study at frequent intervals.

It was found, furthermore, that macrophages obtained from dogs highly immune to the pneumococcus were quite unable to engulf pneumococci without the presence of opsonins. This observation is important in relation to the mechanism of recovery, since it indicates that the macrophages appearing at the termination of the disease are not different from the cells of the normal animal and are dependent on opsonins for their action.

RELATIONSHIP OF MACROPHAGE REACTION TO MECHANISM OF RECOVERY

The data thus far presented, while suggesting the importance of the macrophages in the mechanism of recovery, do not exclude the possibility that the local cellular reaction is secondary to some more fundamental change which affects the pneumococci so that the macrophages can dispose of them. We sought evidence on this point in various ways. Occasionally in the dog suffering from experimental pneumonia, clearing or resolution of one, usually the initial, lesion occurs while spread is taking place in another lobe, a phenomenon sometimes observed in human beings. Half a dozen such animals were killed during the active phase of the disease to determine the state of the lung undergoing this local recovery.²⁶ Cultures from the excised lungs showed that the clearing lesion was sterile while the youngest spreading one contained pneumococci. Sections of the lungs showed in the newest lesion the typical appearance of a spreading process, with great numbers of pneumococci free in the edema fluid, while in the oldest clearing lesion, sterile on culture, a marked reaction of the macrophages was found. No acquired immune substances were detected in the blood of any of these animals, which suggested that the appearance of the macrophages was the determining factor in the process of local recovery.

22. Robertson, O. H.; Graeser, J. B.; Coggeshall, L. T., and Harrison, M. A.: The Relation of Circulating Antipneumococcal Immune Substances to the Course of Lobar Pneumonia: II. Acquired Immune Substances, *J. Clin. Investigation* 13: 633-647 (Aug.) 1934.

23. Robertson, O. H.; Coggeshall, L. T., and Terrell, E. E.: Experimental Pneumococcus Lobar Pneumonia in the Dog: II. Pathology, *J. Clin. Investigation* 12: 433-466 (March) 1933.

24. Robertson, O. H., and Uhley, C. G.: Changes Occurring in the Macrophage System of the Lungs in Pneumococcus Lobar Pneumonia, *J. Clin. Investigation* 15: 115-130 (Jan.) 1936.

25. Curphey, T. J.: Preliminary Report of Intra Vitam Biopsy Studies of the Pathogenesis of Pneumococcus Lobar Pneumonia, *Proc. Am. A. Path. & Bact.* 11: 861-862 (April) 1935.

26. Robertson, O. H., and Coggeshall, L. T.: Local Recovery in Experimental Pneumococcus Lobar Pneumonia in the Dog, *J. Exper. Med.* 67: 597-608 (April) 1938.

However, further observations showed that the process of recovery was of a more complex nature. In an extensive series of autopsies on dogs which had died at different lengths of time after the inception of the disease, a macrophage reaction was found in some part of the pulmonary lesion in the great majority of instances provided the animal lived longer than two days. With few exceptions the reaction became more pronounced and widespread with the increasing age of the pathologic process and was accompanied by a progressive diminution in the numbers of pneumococci, whereas micro-organisms persisted usually in large numbers in the lesions or parts of a lesion where this cellular change failed to occur. In certain dogs which died after four or more days the consolidated lobes were found to be in a well advanced stage of resolution, with the alveolar exudate consisting almost entirely of macrophages, but the animals died with vast numbers of pneumococci in the blood.²⁷ This would indi-



Fig. 3.—Section from the lung of a dog killed four or five days after recovery from experimental lobar pneumonia ($\times 450$) showing subsiding macrophage reaction with a number of free macrophages and others attached to alveolar walls.

cate that the lung possesses great innate powers of recovery. Given a sufficient length of life the lung seems to be able to free itself largely or even completely of the invading pneumococci despite their persistence in the blood stream. It is clear from these observations, however, that the macrophage reaction constitutes only a part of the mechanism of recovery. There is undoubtedly another factor, which may be designated as a generalized process in contradistinction to the local cellular reaction in the lung and which acts to localize the infection and prevent or control invasion of the blood. This general process we may assume involves in part the pneumococidal power of the blood, since loss of this property during the disease is accompanied by bacteremia. There must, however, be other factors operating as well, since occasionally in animals and also in human beings bacteremia occurs despite the presence of pneumococcus-killing activity in the blood.

27. Robertson, O. H., and Loosli, C. G.: A Study of the Macrophage Reaction in the Pulmonary Lesions of Dogs with Experimental Pneumococcus Lobar Pneumonia, *J. Exper. Med.* 67: 575-596 (April) 1938.

Because of our ignorance of its nature we may term this the lung-blood barrier. The mechanism of recovery from lobar pneumonia in the dog so far as we understand it may be indicated as follows:

The mechanism is of a dual nature:

1. Local process: macrophage reaction in the lung + ? local production of immune substances.
2. General process: (a) pneumococcus-killing power of the blood; (b) lung-blood barrier.
 - A. If both processes are effective, recovery results.
 - B. If either process fails, death ensues.
 1. Complete clearing of lungs but pneumococci in the blood = death.
 2. Sterile blood all through the disease but absence of macrophage reaction = death.

ROLE OF ACQUIRED IMMUNE SUBSTANCES

Whether or not acquired immune substances play a significant part in the mechanism of recovery in the dog is not clear, since these substances are not often detectable at this time in the blood of the dog. When they do occur it is subsequent to recovery. We have certain evidence for believing that these immune substances are produced by the cells which give rise to the macrophages, and it may be that they are manufactured in the lung, their presence in the blood indicating an excess production and overflow. Except for the difference in the frequency with which acquired immune bodies are detectable in the blood of human beings and dogs, observations to date would suggest that the mechanism of recovery is essentially the same in the two species.

III. IMMUNITY

Until very recently little has been known concerning immunity following recovery from lobar pneumonia because of the paucity of data on the pneumococcus types which cause recurrent infections. The important contribution of Finland and Winkler²⁸ in 1934 gave for the first time definite information on this subject. They found that one attack of the disease does not confer permanently increased resistance against subsequent infection with the homologous type of pneumococcus but that a second attack of pneumonia rarely occurs within a year. Our studies on experimentally induced pneumonia in the dog showed that one attack confers on the animal increased resistance against a second infection which persists for many months at least. The basis of this heightened immunity appeared to consist principally in a marked acceleration of the macrophage reaction in the inflammatory lesion.²⁹ This study was further extended to include observations on repeated infections in the same lobe versus infection in a hitherto uninvolved portion of the lung, with the purpose of determining whether or not an attack of the disease left the affected part more resistant than other areas. In order to make such tests we infected dogs with very large doses of pneumococcus culture, doses from which the normal animal died with a fulminating disease within twenty-four hours. If this inoculum, 5 cc. of culture, followed by mucin to obstruct its expulsion, was injected into the recovered lobe five days after the termination of the disease the animal survived after a brief and limited infection, while the same dose injected into a previously

28. Finland, Maxwell, and Winkler, A. W.: Recurrences in Pneumococcus Pneumonia, *Am. J. M. Sc.* 188: 309-321 (Sept.) 1934.

29. Coggeshall, L. T., and Robertson, O. H.: A Study of the Repeated Attacks of Experimental Pneumococcus Lobar Pneumonia in Dogs, *J. Exper. Med.* 61: 218-234 (Feb.) 1935.

uninvolved lobe at the same time after recovery resulted in fulminating infection and death, indicating that the factor of high resistance lay within the recovering lobe. If, however, injection into the recovered lung was delayed until two weeks after recovery the dog died. An association between these effects and the presence of macrophages was provided by a histologic study of the lungs of dogs killed at varying intervals after recovery. At the end of five days the recovered lung still possessed a large concentration of interalveolar macrophages (fig. 3). From this period they diminished, until at fifteen days the lung had resumed its normal appearance.

Repeated infection in the same lobe resulted in a much extended duration of the local immunity. After five or six infections the animal survived the test dose, given three to four months after the last attack of pneumonia. But if this dose was injected into a hitherto uninvolved, opposite lobe between fifteen and twenty-five days after the last infection, the animal died. Microscopic examination of the lungs of dogs after recurrent unilateral infection showed in the recovered lobes a certain amount of residual macrophage mobilization, which may have accounted for the prolonged local immunity.

SUMMARY AND CONCLUSIONS

1. By implanting pneumococci suspended in a starch-broth paste into the terminal air sacs it has been possible to produce in the dog a lobar pneumonia which closely resembles that which occurs in the human being.

2. The pneumococci are dispersed from the locus of implantation principally by the edema fluid of the early lesion, which spreads peripherally through the contiguous air passages and the pores of Cohn.

3. The evolution of the inflammatory lesion of the canine disease is essentially the same as that observed in human lobar pneumonia.

4. At the time of recovery a striking histologic change occurs in the pulmonary lesions of both man and the dog. This consists in the transformation of certain of the fixed tissue cells into free macrophages which engulf and destroy the pneumococci much more effectively than do the polymorphonuclear leukocytes. The macrophages are dependent on opsonins for their antipneumococcal activity.

5. The mechanism of recovery appears to be of dual nature, consisting of a generalized process, which acts to localize the infection and prevent or control bacteremia, and a local process, the macrophage reaction, whereby the lung is enabled to rid itself of the invading micro-organisms. If both processes are effective, recovery results. If either one fails, death ensues.

6. One attack of experimental pneumonia confers an increased resistance to subsequent infection which lasts for many months. The basis of such immunity seems to reside in the greatly accelerated macrophage reaction characterizing the recurrent lesions.

7. After recovery a high degree of local immunity can be demonstrated in the involved lobes; it persists only as long as the macrophages are present in the alveoli. However, the duration of the local immunity is greatly prolonged by repeated infection in the same locus. Under such circumstances a residual mobilization of macrophages is observed in the tissues of the lung.

LEPROSY OF THE UPPER RESPIRATORY TRACT

DISCUSSION OF EARLY AND MODERATELY ADVANCED CASES

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Leprous processes may simulate the changes that take place in the mucous membrane affected by subacute and chronic processes of more common occurrence. Though it is believed that the incidence of leprosy is very low in continental United States, there is ample evidence that cases of it are passing through well conducted clinics under improper labels, and the facility with which transportation is carried on with countries of the Pacific, Mexico, Central America and South America foster the introduction of the disease in spite of the screen of ship quarantine inspection.

It has been my privilege and opportunity over a period of seventeen years to observe and study the conditions of the eye, ear, nose, throat and larynx of practically every patient certified as leprosy in whom the diagnosis was proved by painstaking investigation in the Receiving Hospital for leprosy patients at Honolulu, to which an average of from fifty to seventy new patients are admitted annually, and in which there have been between 125 and 200 in residence for periods of from one to eight years. I have also examined, studied and treated large groups of patients among from 450 to 600 in the Settlement at Molokai during these years, by periodic visits of from seven to fourteen days' duration on many occasions.

CLASSIFICATION

The traditional classification of leprosy has been made on the preponderance or presence of clinical evidence and is differentiated by three types, nodular, maculo-anesthetic and mixed. A more current grouping has been made on a similar basis and distinguishes cutaneous and neural cases. During the past two years much discussion has arisen over classifying cases in which there are lesions that have been named tuberculoid lesions or leprides. The clinical type of the case is of interest to the rhinologist and laryngologist because of the accompanying changes in the mucous membranes. However, similar manifestations may appear in cases of different types. The latter observation is in keeping with the view of the authorities who regard the disease as a general infection in which neural, cutaneous and tuberculoid lesions occur and represent only the phases or degrees of the same pathologic process.

PATHOLOGY

The essential histopathologic change of the disease is the involvement of the nerves, skin and mucous membranes by inflammatory processes which are characterized by perivascular infiltration with round cells and

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The extent and degree of the studies and observations in leprosy on which this discussion is based were made possible through the cooperation and assistance of the officers of the United States Public Health Service, who have served as the medical staff at Kalihi Hospital, Honolulu, and the adjoining United States Leprosy Investigation Station. Much of my study has resulted from the stimulating influence, council and advice of Dr. N. E. Wayson, formerly director of leprosy investigation at Kalihi Hospital.

by a localized or diffuse "myxedematous" infiltration in which "foam cells," histiocytes and giant cells occur in varying frequency and number. Distributed through many of these infiltrations, in intercellular and intracellular locations, are single or clustered bacilli which are acid fast to stains. The aggregation of these infiltrations constitutes the granuloma of leprosy, or the leproma. Granulocytic leukocytes are found only infre-



Fig. 1.—Total destruction of septum with sinking in of the nasal tip.

quently in uncomplicated lepromas, and the central necrosis or colliquation which occurs in the granuloma of tuberculosis is rarely seen. The infiltrations appear primarily in the perineural and intraneural supporting tissues, in the deeper layers of the skin and in the tunica propria and submucosal layers of the mucous membranes. As they progress they invade the entire structures and distort or destroy them or, on the other hand, probably through interference with their innervation or nutrition, stimulate hyperplasia or cause them to atrophy. Thus follicles and glands of the skin and glands of the mucosa usually become atrophied, or even completely obliterated ultimately, but may become hyperplastic during a stage of the process. Destruction of the elastic elements and the formation of scar tissue result in a flabbiness and a thinning of the membranes. Epithelium may become hyperplastic, thickened or keratinized, and its appearance suggests that produced by other chronic irritations. On the contrary, it may be thinned out to a single layer of cells which is easily brushed off and leaves a denuded surface. The extension of the process beyond the membranes is of particular interest in the nose and larynx because of the contiguity of the deeper layers of the membranes with the perichondrium of the septum, laryngeal cartilages and stroma of the vocal cords.

The gross pathologic appearance seen in the mucosae is that of thin, pale, dry membranes, diffusely thickened, reddened, soggy membranes or nodular thickenings of similar nature, both with and without ulceration. Invasion of the cartilages mentioned is followed by their atrophy or destruction, as observed in the frequent perforations of the nasal septum.

COURSE

It is characteristic of leprosy to present many acute phases and many spontaneous recessions. In the nose, the disease progresses by stages of activity and recession. A severe acute reaction with nasal blocking, edema and swelling may occur and last for several weeks and be followed by recession to an almost normal condition. During these apparently quiescent periods the nose may appear relatively normal, but close examination will

reveal minor changes of the nature indicated on either the septum or the inferior turbinates. This acute attack may not recur for several weeks or months, but each time it occurs the structures become more and more infiltrated, nodular and ulcerated, and the normal tissues are replaced by the lepromatous mass or, as healing takes place, scars, distortions and narrowing of the passages develop. Similar processes occur in other mucous membranes.

Pain is not a constant symptom in leprosy but may be agonizing and persistent during the acute attacks of leprous fever (leprous reaction) for periods of several days or even weeks. The neuritic pain in the face, arms, hands, feet and back are much more severe than the pain of an acute "break-bone fever."

The onset of leprosy is apparently insidious in most cases but occasionally seems to be ushered in with an astonishing suddenness. Its course, when once it is established, is seldom one of uninterrupted steady progression but rather that of advances and recessions. Probably in few cases are attacks of leprous fever or acute reactions of more or less severe degree escaped. It is to be remarked that even with the advanced and extensive manifestations there is little suffering from pain in other than the attacks of neuritis or arthritis. These may occur during the attacks of leprous fever as accompaniments of the cutaneous eruptions previously mentioned. When present, the pain along the course of the peripheral nerves in the arms, hands, legs and feet may be most severe and resistant to sedatives of such potency as morphine. These acute reactions with neuritis, giant urticaria, cutaneous edema, swollen, bluish red hemorrhagic mucous membranes, eyelids closed by edema, with photophobia and streaming tears are distressingly impressive to the medical attendant. However, they usually persist in such intensity for relatively short periods and are often succeeded by recessions of the lesions and prolonged periods of apparent quiescence, though they may be the initiation of steadily progressive changes.



Fig. 2.—Total destruction of the cartilaginous septum with similar mass of granulation tissue replacing the nose.

It is also not unusual to see very advanced lesions of a more chronic type, which appear to be destined to a chronic and destructive course, subside in a few weeks to such a degree that even a fairly critical examination of the patient by one who is inexperienced may result in failure to detect the disease.

These fluctuations in the course and manifestations in the skin and nerves have parallels in the mucous membranes and structures of the nose and throat.

However, though edema may subside, nodules recede and ulcers heal, there are scars, atrophies, distortions and mutilations remaining in proportion to the severity of the process and to the structure or function of the tissues affected.

CLINICAL OBSERVATIONS

Nasal.—Careful studies of the mucous membrane will reveal that practically every leprosy patient has some nasal lesion due to leprosy. This opinion is concurred



Fig. 3.—Nodular infiltration of uvula with extension into the right supratonsillar fossa.



Fig. 4.—Nodular infiltration of the soft palate.

in by many observers, among them Del Rio,¹ who showed that "the nose was affected in 82 per cent," although he does not state the type of case.

The symptoms that the patient presents are those of dryness, stuffiness, excessive crusting, blocking and epistaxis. All these conditions may be present in modified form in children, but epistaxis and nasal crusting occur most often. The epistaxis may be the most significant complaint to bring the patient to the physician and is undoubtedly influenced by nose picking among children. As the child reaches adolescence, the symptoms are prone to increase markedly, since active leprosy is evidenced more during this period of life and in young adults. Among mature and older adults the symptoms may be those of the complications and sequelae of the more active processes.

The conditions observed within the nose tend to vary in accordance with the predominant clinical manifestations. Among the neural types the mucous membrane is swollen, pale, dry or relatively dry during active progressions, and it is not uncommon to note practical freedom from pain on manipulation of the nasal membranes. Ulceration is not common in the primary neural types, but it does occur in those nodular cases in which healing has occurred and which have become residual or secondary neural forms. Perforation of the septum is frequently found in this secondary neural type, with atrophy and crusting that closely resembles the *ozena* so familiar to all rhinologists. However, there is no assurance that the *ozena* of leprosy is of specific leprosy origin.

Among the nodular types the mucous membranes are markedly reddened, or a bluish gray. They are usually moist but may be dry and present evidence of deep infiltration and nodulation. The membranes impress one as soggy and are covered with crusts, either with or without ulceration, and have a tendency to bleed with the slightest trauma. The principal sites of the nodules are the anterior third of the septum and

the anterior half of the inferior turbinate. They are also found on the lateral walls. The middle turbinates seem to be involved less frequently.

The sinuses do not appear to be attacked by the disease, and I have not seen a case of sinus disease that seemed to be caused by a definite extension of a leprosy process rather than indirectly by the results of the process within the nose or by other conditions. Though the long bones of the hands and feet are frequently included in the leprosy processes, it is uncommon to find the changes in the flat bones such as those of the nose.

Murdock² made a survey at Kalihi Hospital of fifty cases in which there was marked involvement of the soft tissues of the nose but observed no instance of involvement of the nasal bone.

With the cartilaginous septum, however, it is quite different, since large perforations occur in it and extend as far forward as the tip. I have seen several cases in which the entire cartilage had been perforated and destroyed and the nasal tip had become a loose, flabby and formless mass of tissue (figs. 1 and 2).

As healing proceeds, much scarring occurs and may be accompanied by great distortion. The intranasal structures may become adherent by dense synechiae and crusting, and the nasal passages may be completely obliterated. Partial or complete collapse of the alae may result from paralysis of the elevators of the wings and angle of the mouth in lesions of the seventh nerve.

Acute leprosy reactions with marked edema of the nasal mucosa, sudden epistaxis and edema of the face, ears, neck and extremities may occur. These acute reactions are accompanied by high fever, chills, agonizing neuritis and arthritic pains and efflorescence of cutaneous lesions, varying from those of morbilliform character, erythema nodosum or acute cellulitis, and may be complicated by acute swollen nerve trunks and evidence of acute arthritis.

Pharyngeal.—There is a remarkable freedom of symptoms with leprosy involvement of the pharynx unless the patient is suffering with an attack of "acute leprosy reaction." More rarely the palatal muscles may

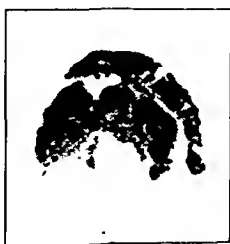


Fig. 5.—Showing the progress forward of the infiltration of the soft palate.



Fig. 6.—Much infiltration and distortion of the entire hard palate.



Fig. 7.—The alveolar processes of the upper central incisors showing extensive involvement.

become progressively paralyzed during the very late stages of the disease and cause the characteristic regurgitation of fluids through the nose and the nasal voice.

Definite changes in the mucous membrane are rarely observed among the neural types. During the acute attacks of leprosy reaction the palatal muscles may become paretic or paralyzed, and with the subsidence

1. Del Rio, A. L.: Clinical Contribution to the Study of Leprosy of the Ear, Nose and Throat, *Ann. di laring., Otol.* 36: 80-88 (Feb.) 1936.

2. Murdock, J. R.: Leprosy: Observations on the Nose and Throat, unpublished paper read before the Honolulu County Medical Society, July 3, 1931.

of the attack there may be an astonishing return of function. Nodular types frequently present changes in the mucous membranes of the pharynx. Nodules commonly occur in the earlier stages at the base of the uvula (fig. 3), extend into the folds above the tonsils and subsequently spread over all parts of the soft palate (figs. 4 and 5). In later stages they spread forward over



Fig. 8.—Large nodular formation of the right half of the anterior tip of the tongue.

the hard palate (fig. 6) and form broad ridges of nodular infiltration along its center even to the alveolar areas (fig. 7). The teeth become loosened and are partially buried by the nodules. On the other hand, the lingual surface of the alveolar processes of the upper central incisors is frequently involved early in this process, and the extension of the infiltration is backward along the ridge of the palate.

The nasopharynx shares in the process by extension, and nodules may be seen high on the posterior nasopharyngeal wall in those cases in which the thickened soft palate does not interfere with examination by the mirror.

Lingual.—Few symptoms are complained of in leprosy lesions of the tongue. Neural involvements of the tongue are not seen, but nodules are (fig. 8), usually in the anterior third and late in the disease. Leukoplakia is also quite common in the same location and occurs late. These areas of leukoplakia are often quite anesthetic to tactile stimulus. Ulceration occurs when nodules have broken down, though they are usually quite superficial. Rao³ describes "macroglossia" in which, instead of definite nodules, the whole tongue may be enlarged owing to a generalized infiltration of the whole organ, which he feels corresponds to the "leontiasis" type of cutaneous lesion affecting the whole face. I have not seen this type of lesion, but I have seen thickened and deeply furrowed tongues (fig. 9), which may be analogous.

Del Rio¹ states that "the tongue was affected in 20 per cent, nodules being observed in 15 per cent and cicatrices in 5 per cent," but my patients have not shown so high an incidence of these lesions.

Tonsillar.—As a result of our studies⁴ and subsequent observations we have concluded that more than 20 per cent of leprosy patients have demonstrable infiltrative and nodular lesions of the tonsils (fig. 10) which are of leprosy origin because of specifically proved associated changes.

Laryngeal.—Approximately 40 per cent⁴ (substantiated by subsequent observations) of the moderately advanced nodular cases present leprosy lesions of some form in the larynx, and in the vast majority of instances the epiglottis is involved. A great majority of the more advanced cases present laryngeal lesions. The characteristic early symptom is "the leprosy huskiness," a

peculiar vocal quality that strikes the experienced as suggestive. The patients complain of a dryness and a tickling sensation that causes a dry, unproductive cough.

The mucous membrane of the neural type is dry and a grayish red, and the surface is often covered with a frosty exudate which is thin enough to allow the red membrane beneath to shine through. It does not become ulcerated as in the nodular type, but it may become atrophied to some extent. The latter observation has apparently been noted also by Sechi and Giunti,⁵ who state that "in neurotic leprosy, however, one will find only the usual atrophic alterations." In the early nodular type the epiglottis is attacked early on both its anterior and posterior surfaces (fig. 11) and extension occurs into the surrounding parts by contiguity along the aryepiglottic folds, the arytenoids and posterior commissure. In early cases the anterior parts appear to be affected first, but in the later stages one may see a dull, gray, nodular tissue within the entire larynx. The arytenoids stand out in the process later by becoming almost immobile, large and hard with infiltrations (fig. 11). Single large nodules form characteristically along the lateral border of the epiglottis. The cords become swollen when nodules involve the lateral bands, as often happens, and the nodules commonly invade the ventricles and vallecula. Nodules in the cords are probably more common than is known, but they are seen rarely because they occur late, when the distortions and infiltrations of the structures above obscure their observation.

The recurrent laryngeal nerve escapes in most cases (except during an acute reaction), while the superior laryngeal nerve is involved more often by deep infiltration in its branches of distribution. I have never seen a case of recurrent paralysis of the nerves which I was sure was due to leprosy. The motor nerves innervating the muscles of the upper part of the respiratory tract are seldom affected in other than very late cases.

Congestion, swelling, infiltration, nodulation, ulceration, atrophy and scar formation with contractures and



Fig. 9.—Broad ridges with deep furrows and islands of leukoplakia involving the entire tongue.



Fig. 10.—Extensive nodular infiltration of the right tonsil.

distortions are the successive steps in the disease in the larynx as in all the other diseased parts of the mucous membrane.

Not infrequently in leprosy patients a severe edema of the larynx develops resembling that of some "allergic" phenomena in intensity and degree. Laryngeal stridor and edema of the glottis may occasionally result in fatal consequences. This acute reaction is also accompanied by high fever, chills, severe pain in the limbs and acute cutaneous lesions of many forms.

3. Rao, G. R.: *Leprosy as It Affects the Ear, Nose and Throat*, Antiseptic 28: 84-96 (Feb.) 1931.

4. Pinkerton, F. J.: *Leprosy of the Ear, Nose and Throat: Observations on More Than Two Hundred Cases in Hawaii*, Arch. Otol. 16: 469-487 (Oct.) 1932.

5. Sechi, E., and Giunti, G.: *Leprous Laryngitis*, II, Valsalva 7: 824-842 (Nov.) 1931.

DIAGNOSIS

Though the diagnosis of leprosy can be made in many instances by clinical examination, it can be confirmed in most cases by bacteriologic examination. This can be made easily and quickly by the rhinologist with microscopic preparations.

The technic of making a nasal "snipping," which follows is comparatively simple: Use a semisharp

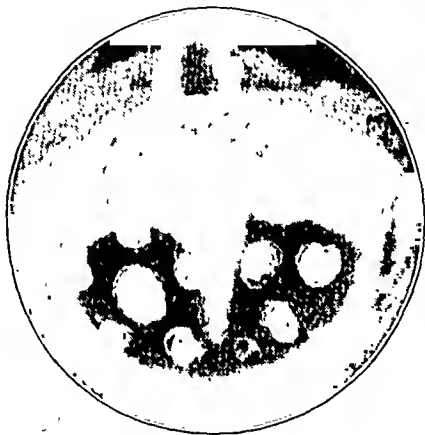


Fig. 11.—The epiglottis infiltrated with nodules throughout its entire anterior and posterior surface and the arytenoids extremely enlarged and infiltrated with hard nodules.

Freer submucous elevator under good illumination, press firmly enough to blanch the tissues under the blade and scrape hard enough to get some of the epithelium, since the bacteria are in the tissues; hence swabs collecting mucus are valueless unless ulceration is present. Spread the collected scrapings on a slide and stain by the Ziehl-Neelsen method of staining for tubercle bacilli. The favorite site for scraping is the septum, near the anterior border, or on the side of the nose immediately above the anterior end of the inferior turbinate. Blood in the specimen makes a poor microscopic preparation, and the attendant trauma may leave an intractable ulcer; hence bleeding should not be provoked.

Murdock² examined 164 patients by the foregoing method and 143, or 87.2 per cent, gave positive bacteriologic results, which is a higher percentage than would give positive results with cutaneous snips.

The same technic may be carried out when practicable in the examination of the pharyngeal lesions. When a well defined nodule exists in the soft parts, any form of ring punch may be used to remove the entire nodule for biopsy. This procedure may excite an intractable ulceration which might not otherwise occur; hence excision of a nodule of the mucous membrane should be resorted to only in unusual cases.

As a rule I depend on swabs for collecting bacteriologic specimens from the larynx. I have used the punch on nodules of the epiglottis, but here again there is the danger of starting up an ulcerative process.

In the event that these examinations of the nose and throat are undesirable, because of any of several reasons, contributory evidence of the presence of the disease may be obtained by "snipping" the skin of the lobe of the ear, even though no definite changes are detected in it. Snippings from the ear are easily carried out and yield reliable results if properly executed. I have found the best technic to be as follows: Grasp the lobe of the ear or the nodular area firmly between the thumb and finger of the left hand to blanch the tissue; have an "ever-ready" reinforced back safety razor blade with a single cutting surface in the right hand; with the toe or point of the cutting edge, make a small nick into the area about 3 mm. deep, and while the blade is still buried in the tissues twist it out at right angles to the line of incision, carrying with it some serum and tissue cells wherein the bacteria are located.

In the event of failure to confirm the diagnosis in suspected cases by examination of the local lesions and the ear, one should make an inspection of the entire body, looking for associated lesions and making microscopic examinations of those cutaneous lesions observed. The skin of the brow and of the buttocks is affected very frequently, and the lesions found in these areas are often more advanced than those in other locations.

DIFFERENTIAL DIAGNOSIS

Leprosy is commonly mistaken for syphilis and until later years it was common experience to find that leprosy patients had had much antisyphilitic treatment before a diagnosis was finally made. This mistake was made because such a great number of leprosy patients gave a positive Wassermann reaction. More than 40 per cent of leprosy patients show a positive Wassermann reaction in the nodular types without a history or other evidence of syphilis. I have observed negative Wassermann reactions on admission of leprosy patients to the hospital and have also observed that as the leprosy disease progresses the Wassermann, Kahn and other precipitation tests become positive and that the intensity of the test diminishes as the leprosy recedes. In the U. S. Public Health Service conference in which serums were submitted to Kolmer, Kahn, Eagle and originators of other tests, the results were as described.

Wayson,⁶ who studied the subject at Kalihi Hospital, thinks that "most cases of advanced nodular or myxedematous types will yield positive serology." No evidence has been submitted to prove that patients with the neural type (except those secondary to the healed nodule) give more positive tests than other members of the general population of the same age, race and manner of living.

The therapeutic test may be resorted to in doubtful cases, but even this is not proof of syphilis. In the administration of arsenicals the leprosy condition may recede as in syphilis, though much more slowly. However, leprosy frequently recedes spontaneously without therapy of any sort and likewise after administration of intravenous treatment with nonsyphilitic agents.

A detailed word picture of the appearance of leprosy changes in the mucous membranes is difficult and one unconsciously forms conclusions from clinical "hunches" and experience with numbers of cases of the two other diseases whose underlying pathologic condition is classified as a granuloma, namely syphilis and tuberculosis. I have had limited experience with laryngeal syphilis but have been fortunate through my association as attending laryngologist to an active hospital of 450 beds for tuberculous patients to be able to make comparisons between the tuberculous and the leprosy process. Then too, many leprosy patients have tuberculosis. In



Fig. 12.—Advanced nodular infiltration with destruction of the central portion of the epiglottis.

6. Wayson, N. E.: Personal communication to the author.

fact it is a common coincident infection and the two diseases are frequently present at the same time.

Leprous, tuberculous and syphilitic lesions of the larynx may resemble one another at one stage of their development.

Tuberculosis almost always involves the posterior part of the larynx first, and the most frequent site is the posterior commissure. The arytenoids, folds and epiglottis are involved later.

Leprosy involves the epiglottis first and the cords and arytenoids later. The anterior and the posterior surface of the epiglottis are affected alike. Tuberculosis is almost always very painful while leprosy is characteristically almost painless. In the earlier stages the mucous membrane is more hyperemic in tuberculosis and syphilis, while in leprosy it is pale and gray. Tuberculosis is bilateral as a rule; syphilis is usually unilateral and almost always involves the anterior structures, while leprosy may be either and when seen late is widespread, involving several parts. Syphilis quickly ulcerates, the ulcer being sharply defined with clearcut edges, the surrounding areas being smooth and highly congested. The larynx wherever involved with leprosy is definitely nodular, though ulceration may occur. When ulceration occurs, aided by secondary infection, the epiglottis may be destroyed (fig. 12). However, one does not see the great destruction of tissue in laryngeal leprosy that one sees in tuberculosis or syphilis, with the same amount of nodular involvement. Leprosy tends to heal, and scars cause distortions in one area while the adjoining area is actively infiltrated with nodules. A leprosy larynx may be intensely nodular and infiltrated and not break down, while in tuberculosis and syphilis no such extensive nodular infiltration takes place without early deep ulceration and breaking down.

While a differential diagnosis can be made in most cases, there are times when all local signs fail and one

must depend on examinations elsewhere in nerves, skin and chest and in serology and bacteriology.

Care must be observed in making the bacteriologic diagnosis and it is sometimes necessary to resort to bacteriologic cultural methods, since staining and morphologic characteristics are not sufficiently exact to differentiate the bacillus of leprosy from that of tuberculosis.

Even animal inoculation may be misleading since the development of large lymph nodes containing acid-fast organisms may occur after inoculation with either of these bacteria. *Bacillus tuberculosis* grows readily and characteristically on suitable mediums. The bacillus of leprosy has probably never been grown on artificial mediums.

The presence of nasal deformities present striking differential points. I speak of the so-called saddle nose.

If the bony septum is destroyed and absorption of the nasal bones occurs in syphilis, one may expect to find a sinking in or depression of the nose (fig. 13).

In leprosy the bony septum is not destroyed; only the cartilaginous portion is involved, and in this type the nose sinks nearer the tip (fig. 14).

It has been reported that the hard palate may perforate, but I have never seen a case which I considered



Fig. 14.—Leprous deformity of the nose characterized by destruction of the septal cartilage and sinking in of the nasal tip.

was due to leprosy; syphilis yes, tuberculosis perhaps, but leprosy no.

TREATMENT

After having tried many of the remedies, including the heralded chaulmoogra oil, I have concluded that none of them act as a specific in local or topical treatment. Hygienic care of the mucous membranes, which resolves itself largely into methods of cleansing, and the accomplishment of drainage in the nose appear to assist uncomplicated healing and certainly give comfort to the patient. This general conclusion was reached after controlled experimental treatment which I carried out several years ago⁴ on another large group of patients and has seemed to be substantiated by subsequent observations.

I have found that the patient who rests his larynx has less cough and irritation than one who indulges in talking and other vocalizing which amount to abuses of his larynx. I have used the spray of chaulmoogra oil directly into the larynx without favorable results. The use of bland oils by inhalation of the fine spray seems agreeable to the patient. Finally, the treatment of leprosy of the upper part of the respiratory tract is much the same as that of treating the same parts in a tuberculous patient, and, since the condition of the nose, throat and larynx reflects to a great extent the general condition of the patient, the treatment should in the main be directed toward improving the general condition.

ABSTRACT OF DISCUSSION

DR. R. W. BURLINGAME, San Francisco: Having had the privilege of caring for the lepers for the San Francisco health department for the last twenty-one years, I find the observations on leprosy of the mucous membranes of the nose particularly interesting. These membranes are an aid to diagnosis and have been discussed for the past forty years, first by Stecker in 1897 at the International Leper Conference held in Berlin that year and later by Plummet, Falcao, Brinkerhoff, Holman and others. I believe this is the first report of so many cases over such a long period by a trained rhinologyologist. Most of the earlier reports deal with the finding of the lepra bacillus in the nasal secretions; others advance the theory that the initial lesion of



Fig. 13.—Characteristic nasal deformity, saddle nose, due to syphilis.

leprosy occurs in the nose. Dr. Walter Brinkerhoff's conclusions were that examination of the nasal septum was of no value in the diagnosis of incipient leprosy. I believe that not a few lepers might be discovered early in the disease by nasal examination in nose and throat clinics dealing with Islanders, Orientals, Central Americans and East Indians, were the findings of Dr. Pinkerton kept in mind. This is important from a public health standpoint, as this is the most infectious period of the disease. Fortunately, with one or two exceptions, European races in the temperate climates have built up a comparative immunity against this disease. On at least two occasions in the last few years we have received lepers at the Isolation Hospital, where the tentative diagnosis was made in nose and throat clinics in which the patient applied for treatment because of nasal symptoms alone, there being nothing on the exposed surfaces of the skin to suggest leprosy at the time of examination. After the disease was found in the nose and acid-fast organisms were demonstrated by the microscope, a more thorough examination with the patient undressed disclosed well defined macules and ulnar nerve enlargement of early neural leprosy. These very early cases are usually of the neural type and are not noticeable until the patient is undressed, because the usual contractures and deformities of the hands have not had time to develop, whereas the nodular or cutaneous type of leprosy usually occurs on the ears, face, brows or neck, where it is plainly discernible before nasal symptoms become troublesome.

DR. RALPH A. FENTON, Portland, Ore.: It is unfortunate that time limitation made it impossible for Dr. Pinkerton to give this splendid paper in its entirety; I think it should be read by all of us on the Pacific Coast who happen to be seeing people who come off the various vessels that come across the Pacific or from the South Seas. It is particularly important to us. It is also important to men who are practicing in New Orleans or in Texas and the Gulf ports. A good many of these cases slip by. They are picked up by the United States Public Health Service occasionally, but it is very important that the summation of the work of twenty-five years that Forrest Pinkerton has given should have a prominent place in the literature and should become a bible to those of us who practice in the seaports of this region.

DR. FORREST J. PINKERTON, Honolulu, Hawaii: I should like to stress the point Dr. Burlingame brought out. We are not concerned with the diagnosis of the advanced case. The layman on the street does that. The doctors are guilty of allowing these patients to go on misdiagnosed for a matter of months. In my paper I refer to that. It has been common experience to find patients who have been treated for syphilis for a year or two years during these earlier stages of the disease. The positive Wassermann reaction is used often as a single criterion in diagnosing syphilis, but it is known that approximately 40 per cent of leprosy patients will show a positive Wassermann reaction at one time or another without a history or other evidence of syphilis. Another thing that should be stressed, as Dr. Burlingame brought out, is the importance of stripping the patient: undress him, do not use artificial light, use good daylight and you will be surprised what you see when examining these unexplained lesions; you may discover other infiltrative lesions around the area of the malar eminence and commonly on the buttocks, the favorite sites for the macular types. The anesthetic type, of course, is more difficult and one must use the tactile heat and cold technic and all the other finer techniques that come from special study.

Thyroxine the Watchdog of Metabolism.—Less than a thousandth of an ounce of iodine is all that stands between you and imbecility. It is the principal constituent of thyroxine (distorted from the Greek, meaning "I rouse to activity") which is the watchdog of metabolism. Without thyroxine we should be as brainless and inactive as vegetables and far less beautiful, and it takes iodine to make thyroxine. If the soil contains enough iodine there is an ample amount in the food. In places where the soil is deficient in iodine the food and water are also deficient, and the inhabitants have goiter.—Furnas, C. C., and Furnas, S. M.: *Man, Bread and Destiny*, New York, Reynal & Hitchcock, 1937.

THE PSYCHOANALYTIC TREATMENT IN A SANATORIUM OF CHRONIC ADDICTION TO ALCOHOL

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There is perhaps no other condition met in psychiatry in which there is so much confusion of treatment methods, so much interference by the relatives and so many cases of relapse after attempted treatment as in chronic alcohol addiction. Also there is perhaps more pessimism with regard to this condition among those who attempt the treatment of unselected alcoholic addicts than with regard to any other psychiatric condition. Those who, like the laymen-therapists Durfee, author of "To Drink or Not to Drink," and Chambers, co-author with Dr. Strecker of "Alcohol—One Man's Meat," elect to treat only those addicts who themselves desire and seek treatment and are willing to cooperate, are still able to discuss the subject optimistically, but they give no evaluation of statistical results over a period of time. This paper will deal with the attempt to apply psychoanalytic knowledge to the study and institutional regimen of chronic alcoholic addicts and psychoanalytic technic to the individual treatment of such patients. I shall not attempt a statistical summary of all cases treated at this institution (the Menninger Sanitarium) but shall confine myself to my personal experience with twenty male alcoholic addicts seen in the past five years, of whom eleven were in psychoanalysis for varying periods.

SELECTION OF CASES AND ADMISSION TO THE SANATORIUM

There has been no selection of favorable cases in the series on which this discussion is based. There is an implicit selection from a certain social and financial stratum, however, since only those patients are dealt with who can afford, or rather whose parents can afford, moderately expensive institutional fees. Nineteen of the twenty patients came under pressure varying from parental insistence and threats of divorce action by their wives, which resulted in pseudovoluntary admission, to being brought by force by relatives, physicians and attendant, or deputy sheriff, often by deception, and deposited drunk in the institution. With these intoxicated, unwilling patients it is our policy to begin immediate medical care directed toward whatever physical condition is found, with immediate withdrawal of all alcohol. The psychiatric struggle begins when such a patient begins to sober up. His typical reactions of anger at incarceration, demanding of freedom and privileges, and protestations that he has now learned his lesson and won't drink any more are met with the consistent attitude on the part of physicians, therapists and nurses that his history clearly indicates a need for psychiatric study in a controlled and restricted environment and that such freedom as we may be able to give him later will depend on such study and observations. This period of "beating against the bars" may last from a few hours to many weeks, but however long it lasts the same consistent attitude is maintained toward him, and attempts are constantly made to obtain his own history, as detailed a history as possible having already been secured from relatives or the referring physician.

From the Menninger Clinic.

Read before the Section on Nervous and Mental Diseases at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 15, 1938.

If, as rarely occurs, an alcoholic addict with his own financial resources comes to the institution seeking treatment, he is told frankly of the restrictions that will be a part of the treatment and is bluntly informed that he will not like it and will want to leave. He is also told that any adequate treatment will require many months. If he decides to enter, knowing such factors in advance, the outlook is better, because half the battle is won if there is a sincere desire for help.

PSYCHIATRIC STUDY AND EVALUATION OF THE CASE

It is recognized by all psychiatrists who have studied persons chronically addicted to alcohol that the alcoholism is only a symptom, not a clinical entity, and that while there are certain personality traits common to most alcoholic addicts, the drinker's deeper psychologic conflicts and environmental distress are strictly individual and vary as widely as do similar factors in various neuroses and psychoses. Superficial impressions to the contrary, no excessive drinker is normal and well adjusted when sober. It is the purpose, therefore, of the period of psychiatric study to discover what the individual aspects of the problem are for this particular person and to evaluate the severity of the addiction and the possibilities for reconstruction of the personality in his case.

In previous papers I¹ have attempted to assay these factors. In general one may expect to find a parental background characterized by inconsistency and lack of unanimity of parental discipline, resulting in conflicting, unstable identifications in the son. One parent, usually the mother, has always been overprotective and over-indulgent, shielding the son from the father's severity; the father has usually been inconsistently severe and indulgent, with considerable lack of real affection expressed and many clashes with the mother over discipline of the son. Such overindulgence combined with later sterner expectations and demands is, of course, more likely to occur in families of the well-to-do or wealthy class, from which the patients comprising this study are drawn. Innumerable personality shadings and accents are possible from a son's reaction to such parental management, but one regular result seems to be the fostering of excessive passive demands and expectations in the son—such passive, childish, feminine wishes being in marked conflict with masculine strivings inculcated by the father and by the cultural ideology absorbed from schooling and from contacts with other males. Excessive drinking supplies a compromise solution to both aspects of this conflict. It affords implicit gratification of passive oral wishes, and, at the same time, through the distorted standards of masculinity of late adolescence, provides the illusion of being masculine through his trying to be a hard-drinking he-man who can "hell around" with the boys. The same distorted conception of masculinity leads such boys into early heterosexual promiscuity in spite of the varying degrees of impotence caused by their conflict. I have labeled "essential alcoholics" those patients in whom one can discover plainly the evidences of oral fixation and passive, feminine wishes conflicting with masculine strivings, solved on contact with alcohol during adolescence by excessive drinking, with inability to carry on any sustained effort in school or in a job. They are

called "psychopaths" and are not even accepted for treatment by some therapists; and indeed their prognosis is bad, for a therapist has great difficulty in offering them a reality of sobriety and achievement which compares in satisfaction with their irresponsible dependent state. Treatment of such cases seldom lasts long anyway, since, becoming dismayed at the long road they must travel, they quit, on one pretext or another, or talk their relatives into believing that they are being badly handled or that they are now "cured." One finds that their main goal all along had been to attain through psychoanalysis a magically omnipotent state with ability to continue to drink, to have all the pleasures of drinking with none of its unpleasant after-effects.

A second more hopeful group may be called "reactive alcoholics." They are differentiated from the essential alcoholics by the facts of the history as much as by their attitude toward treatment. In nearly every case there is a discoverable precipitating event which initiated the severe drinking. Often their drinking is periodic, the sprees being reactions to reality stress. They have achieved more, have exhibited the capacity to carry through a sustained effort in schooling or in jobs, and their attitude toward treatment is more sincere. If their relatives do not interfere and interrupt the treatment prematurely, the outlook for them is good, unless their drinking has done too much damage to their reality situations that cannot be undone.

A third group might be called "symptomatic alcoholics." With these patients the drinking is only incidental, not the major symptom. There are other prominent neurotic or psychotic symptoms or even an organic illness. The diagnosis and prognosis of these patients depend on the main psychopathologic condition found.

TREATMENT

Combined institutional treatment and psychoanalysis is the treatment of choice in most cases of intelligent addicts to alcohol who sincerely want help. To say that institutional treatment is based on psychoanalytic principles means only that the activities of the patient and the attitudes of the doctors and therapists are "prescribed" on the basis of the discerned unconscious needs of the patient. Outlets for aggressive drives are prescribed and provided, anxiety is made endurable during periods of distress, and praise and affection are given at appropriate times. In other words the staff and nurses become wise, fair and moderately indulgent but consistently firm parents during the period of sanatorium care. Practically, this is carried out by having a psychiatrist other than the analyst take charge of the patient's privileges and regimen, with this psychiatrist and the analyst acting as checks on each other in relation to the patient's progress in analysis and his daily behavior. Detailed order sheets indicating attitudes to be assumed are prepared for the nurses and therapists, and these are frequently revised to meet new problems with the patient. When the patient has graduated from complete restriction to almost complete freedom with regard to privileges to come and go and has demonstrated his ability to handle the freedom given him, he may move out of the sanatorium and continue his analysis while living in an environment which is unsupervised.

Psychoanalytic treatment, directed at the searching out and working through of unconscious conflicts, with considerable reeducation involved, offers no magical or

1. Knight, R. P.: *The Psychodynamics of Chronic Alcoholism*, J. Nerv. & Ment. Dis. 86: 538 (Nov.) 1937; *The Dynamics and Treatment of Chronic Alcohol Addiction*, Bull. Menninger Clinic, September 1937, vol. 1, No. 7.

miraculous therapy. It depends always on the patient's motive power to go ahead. This motive power may be strengthened by wise handling, by being reenforced with a desire to please the analyst or by the better perspective and more attainable normality glimpsed through the psychoanalytic work, but fundamentally one can help the patient only so far as he continues to want and seek help in working out his conflicts.

Much of the content of psychoanalytic treatment is similar to that of other types of therapy in which the therapist strives through reeducation and interpretation of personality reactions to bring the patient to a better life adjustment. The chief difference lies in the attempt in psychoanalysis to follow the transference reactions and to choose the optimal time for the interpretations and reeducation in relation to the transference situation. In many descriptions of psychiatric treatment one gets the impression that the interpersonal relationship of patient and psychiatrist is almost completely ignored—except as the valuable leverage of the patient's confidence and trust and desire to please may be recognized. It is much more important for the psychiatrist to be able to perceive the evidences of distrust, of hostility, of need for affection and so on as they are portrayed in the nuances of the patient's speech and behavior. Interpretations and questions of the analyst are based on the perception of these transference manifestations, and the whole course of the interpretative content is based on and timed by such observations by the analyst. This, it seems to me, is the common sense as well as the chief distinguishing characteristic of psychoanalytic treatment.

RESULTS

One can work out the most rational understanding type of treatment and sanatorium management possible and still have it go on the rocks and be futile. This is especially true in attempting to deal with alcoholic addicts. There are two main rocks on which the treatment is shipwrecked: first, the flagging desire for help on the part of the patient, owing to his mounting resentment at the lack of satisfaction of all his childish demands; and, second, the interference of the relatives. Because alcoholic addicts have so many demands for gratifications and for having their own way, they have usually developed "winning ways" and various devices for getting their relatives to accede to their wishes. This interaction of parental inconsistency and patient's demands has become the very warp and woof of the alcoholic addict's interpersonal relationships. So it is that the alcoholic addict can again, when he becomes displeased with his treatment, persuade his parents or wife to rescue him from his unpleasantness or can provoke them, through his behavior, to refuse to spend any more money on him. The relatives want to believe what the alcoholic patient protests to them—that he has now seen the error of his ways, even though they may have been disillusioned on that score many times before. One can sometimes circumvent this by prophesying such a situation at the outset and by educating relatives to understand what is going on, but many times they will pay only lip service to these pronouncements and be taken in again by the promises of the patient.

A condensed summary of the results of attempted treatment of this series of twenty patients follows:

1. An oil promoter aged 32, who had scarcely drawn a sober breath for fifteen years, was brought drunk to the sanatorium against his will. He stayed for one month and had thirty daily

conferences of an hour each. He gained considerable insight and remained sober and achieved much for six months after he departed. He then relapsed badly.

2. A reactive alcoholic addict aged 29 was consulted as an outpatient during one of his sprees. He was seen ten times during and following the spree and made a good readjustment. When last heard of two years later he was doing well.

3. A reactive alcoholic addict aged 36 was brought in drunk by his irate, unreasonable father, and was seen twenty times during and subsequent to his sanatorium residence. His father took him out after a week, but the patient sought further consultations and made a good readjustment, which survived his father's death. He was doing well when last heard of a year after the treatment.

4. An essential alcoholic addict aged 35 was brought in drunk by his indulgent father and removed after ten days, against advice. He was seen ten times with no results and continued to drink.

5. A physician aged 34 came sober and voluntarily after he had beaten up his wife while drunk and she had left him. He was an outpatient, was seen six times in consultation, gained some insight and planned to have psychoanalytic treatment when he could arrange it. Four months later he was still refraining from drinking, had gotten his wife back, and was pointing toward the beginning of psychoanalysis.

6. A Jewish essential alcoholic addict aged 38 was seen for twenty analytic hours during the absence of his regular analyst. After some 200 hours with the other analyst, during the latter part of which he was making a fair adjustment as an outpatient, he provoked his relatives into removing him to another sanatorium, where he has now been for eight months, without privileges.

7. An attorney aged 46, a symptomatic alcoholic addict, who had lost one eye in an accident, never became very accessible in sixteen hours of psychotherapy but did no drinking during several weeks of complete privileges. He was removed by the relatives, relapsed in three months and was placed in another sanatorium.

8. An essential alcoholic addict aged 30 caused no trouble during two months of sanatorium residence but was never quite "sold" on the need for psychoanalysis. He was seen in two interviews and decided against psychoanalysis. He persuaded his father to remove him and there has been no follow-up report on him.

9. A capable newspaper man aged 34 became a voluntary patient after he became unable to do his work without heavy drinking, the situation being complicated by the loss of his little son in an accident. He was seen in twenty analytic hours and then referred to another analyst in a city where he could get a job. He is steadily improving, even though his wife deserted him when certain expected benefaction failed to materialize.

10. A divorced man aged 34, who had quit drinking two years before and who had made a serious suicidal attempt prior to that, came for psychoanalysis because of lack of ambition and inability to concentrate. There was a complex neurotic picture with much acting out which seemed to be equivalent to his former alcoholic sprees. He had forty-five psychoanalytic hours as an outpatient, during which he secured a job in another city and then left treatment. He worked hard, did well, and on the day he was promoted to a more responsible position died of an attack of coronary thrombosis.

11. An essential alcoholic addict aged 32, divorced, was brought in drunk, refused to cooperate during the first two months, and then began psychoanalysis. During 160 hours of analysis he was in and out of the sanatorium several times because of drinking and never gave up the hope of being able to drink like a gentleman. When it was finally insisted that he remain in the institution long enough to make some progress in his analysis before trying outpatient status again he balked and got himself released by habeas corpus action, which was not contested. He has continued to drink heavily.

12. An essential alcoholic addict aged 40, who had been declared incompetent and was brought to the sanatorium drunk by two deputy sheriffs, refused psychoanalysis for two months

and then began treatment. During 240 hours of analysis he improved greatly in his behavior and made a good adjustment as an outpatient. However, he continued to refuse to discuss his extremely maladjusted sex life and finally quit treatment. A few weeks later he had a severe spree complicated by an epileptic attack with severe head injuries and ensuing pneumonia. He recovered from this and was placed on a farm by his relatives, where he is now doing fairly well.

13. A playboy son aged 32 of a severe, eccentric millionaire father and a deceased mother who was schizophrenic the last fifteen years of her life remained in psychoanalysis for sixty-five hours with no drinking on full privileges, then easily persuaded his father to spend no more money on treatment. Six months later he was still doing no drinking.

14. A boy aged 27 with esthetic temperament was being forced by his father into the banking business and the boy reacted by drinking heavily. His mother had been a heavy drinker for many years. After the boy had made considerable progress in ninety-five hours of analysis and I was away on vacation his father announced to him that he must now shift for himself—no more treatment, no more financial help. He reacted with severe drinking and his wife left him. The patient was well on the way to recovery when the father interfered.

15. A reactive alcoholic addict aged 32, a capable mining engineer, entered the sanatorium drunk but cooperated well and made an excellent adjustment as an outpatient during the latter part of 157 hours of analysis. An attempt to try himself out at drinking again developed into a severe debauch, from which he was extricated without institutionalization again. He then decided to strike out for himself in the mining game in Bolivia and for two years has done exceptionally well, doing no drinking.

16. A severe essential alcoholic addict aged 28, and unmarried, remained in a stormy analysis for more than 300 hours, quitting when I left on a summer vacation. He has done some drinking in the eight months since but has stuck close to his new job and has gotten into no trouble.

17. A reactive alcoholic addict aged 30 with marked schizoid personality traits stopped analysis after 470 hours, having made a moderately good adjustment. The death of his father during analysis and the continued heavy drinking of his mother, together with his being surpassed in the family business by his rival younger brother during the patient's absence, complicated an already difficult analysis. He left convinced he must remain a teetotaler and hopes to return for more analysis later when drinking is not a part of the picture.

18. A reactive alcoholic addict aged 28 made a good outpatient adjustment after several months of combined sanatorium care and psychoanalysis. The family physician persuaded his father to stop the analysis after 160 hours and the patient has since made a good adjustment.

19. A reactive alcoholic addict aged 40 was seen in consultation four times. His severe drinking was precipitated by the wild antics of his wife after he had made a fortune in wheat. She divorced him and refused to let him see the children. He stopped drinking, took his children and their friends and his ex-wife on a trip to New York, was reconciled to his wife and remarried her.

20. A lawyer aged 30, an essential alcoholic addict, has been in analysis only twenty-five hours at this time but offers a good prognosis for recovery.

SUMMARY

This report is based on personal experience with twenty male alcoholic addicts, with whom I have spent a total of about 2,000 hours. Eight of these were not in psychoanalysis and three of these eight were not in the institution. Consultation hours varied in number from two to thirty. Two patients were unchanged, two relapsed after periods of three months and six months respectively, and four remained improved when last heard from but have probably relapsed. Of the remaining twelve who were treated psychoanalytically, one

was a former alcoholic addict who had stopped drinking two years before of his own accord and who was not in the sanatorium. The other eleven received combined sanatorium care and psychoanalytic treatment, the latter lasting from sixty-five hours to 470 hours. Two are still in analysis, one with me and the other with another analyst. The treatment of four patients was stopped by the relatives, one remaining slightly improved, one relapsing badly in reaction to the interference and two remaining moderately improved after some months. The other five patients stopped their own treatment for various reasons. Of these one was unimproved, three were moderately improved and one much improved.

I have tried to summarize the evaluation and classification of chronic alcoholic addicts and to indicate the rationale of combined sanatorium treatment and psychoanalysis. The difficulties in carrying on this plan of treatment long enough to effect permanent changes in the patient are enormous, not only because of the lack of a powerful enough urge to recover in the patient but also because of interference by the relatives. It has been conclusively proved by the experience of every therapist of persons addicted to alcohol that no individual who has for any considerable time used excessive drinking as a regressive method of avoiding facing his problems can ever hope to learn to drink socially. Sanatorium care to control his drinking for a few months and to provide a rational program of activities and outlets to meet his particular unconscious needs, combined with psychoanalysis which continues for several months after he has left the sanatorium, seems to be the most rational plan of treatment. Such a program should, depending on the severity of the case, last from eighteen months to three or four years.

ABSTRACT OF DISCUSSION

DR. F. G. EBAUGH, Denver: Alcohol and man present a wide variety of equations, most of which in our present state of ignorance seem insoluble. It may be wise to consider this from three points of view: 1. The impersonal or somatic point of view. Time does not permit discussion of the physiologic and morbid aspects of alcoholism, although recent advances in respect to the avitaminoses has led to a clearer understanding of some of the somatic residuals encountered in alcoholism. 2. The personal or point of view of the personality. I am in accord with Dr. Knight when he states that alcoholism is a symptom of some type of fundamental underlying personality disorder and that remedial measures to be effective must be directed at causal factors. 3. The interpersonal aspect, namely that of appreciation of the relationship of the patient to his environment. Sociologically, alcohol presents a tremendous problem. In the United States there has not been an adequate study, from a psychiatric point of view, of facilities and methods in use for the care of the chronic alcoholic addict. Fleming's review of the problem in England and on the continent reveals a marked disparity in methods of attack and attitudes of state, law and medicine. There is a need for a critical psychiatric and sociologic study of the alcohol problem in this country. I have utilized a diagnostic scheme somewhat varied from that suggested by Dr. Knight. I have divided those alcoholic addicts whom I have treated into five principal classes. But before this it may be wise to define what is meant by an abnormal drinker. Strecker's statement that drinking becomes abnormal when one drinks to excess in solitude and to escape reality is valuable. By situational alcoholism I mean those who are not overt, neurotic or psychotic and those who have graduated from the socially acceptable cocktail to abnormal drinking as a result of stress or strain environmentally. In my second group, alcoholism in relation to a true neurosis is self explanatory. Alcoholism simplex is a much more complex type, in which I believe the patient presents addiction to alcohol as an only symptom which

in itself may be a symptom of a deep-seated neurosis. This type of patient presents evidence of some type of psychosexual arrest. This may be similar to Dr. Knight's essential alcoholic. In the fourth group are the psychopathic personalities. In the fifth group, alcoholism is associated with a major psychosis, the defective disorders, schizophrenia and the organic reaction types. Treatment is most difficult. In addition to the two points stressed by Dr. Knight, one should not forget the financial factor, that of the need for adequate hospital study, which is rarely possible in most of the cases.

DR. KARL MENNINGER, Topeka, Kan.: In my earlier years in psychiatry I looked on alcohol addiction as a bad habit and a little later as a neurotic manifestation, one which was peculiarly annoying to the relatives and self destructive to the individual but one which ought surely to be accessible to various types of psychotherapy. Now I regard it as near a psychosis. I dare say some of my patients subsequently fall into the hands of other psychiatrists and I am sure that the patients of other psychiatrists come to me because the characteristic thing about the psychiatric picture of addiction to alcohol is that the patients have fluctuating periods of anxiety between which they feel relatively comfortable. When they have acute anxiety they drink and then they are not accessible to treatment; when they cease to have anxiety they do not want treatment, and that makes alcoholism an extremely difficult problem. I think that addiction to alcohol is more serious than any neurosis and should be thought of along with the psychoses. I think that the prognosis in schizophrenia is better than the prognosis in alcoholism. I would be inclined, if one of my young relatives had to have either schizophrenia or addiction to alcohol, to believe that his chances for getting back into a normal life would be greater if he had schizophrenia. If one treats alcoholic addicts only by letting them get over an acute attack and waiting until they promise not to drink any more, one can easily believe that what I have said is exaggerated. I used to think that too until I became increasingly careful with my follow-up system. Many alcoholic addicts have such strongly fraudulent characters that their wish to deceive the doctor is only a part of their wish to deceive everybody and to obtain relief from their anxiety in the way which they have found is the cheapest and most available. Dr. Knight's paper represents work that he has been doing for a number of years. It does not make any claims for extraordinarily good therapeutic results. My results are not very encouraging, any more than the treatment of schizophrenia is particularly encouraging. Some patients get well if one spends enough time with them, but the temptation is to think they are well simply because they have left with good promises. I agree with Dr. Ebaugh; we should make a concerted and persistent effort to be as scientific as possible in our investigation of what alcoholic addiction really is as a psychiatric syndrome and how it can be treated effectively.

DR. EDWARD E. MAYER, Pittsburgh: The reality situation of the privileged is slightly different from that of persons who are not protected by family and friends, and it is in respect to the latter class that I would like to say a word in respect to treatment. At a clinic that is municipally controlled and has one of my associates daily in attendance at the morals court, a large number of alcoholic addicts is examined. Those who he believes should have any psychoanalytic interpretation are given an appointment at the clinic. It is not a conscious reality that the alcoholic addict is evading or avoiding. Or put it this way: there are many realities in any group situation involving a particular individual. It is the interpretation of them that is important. Of course Dr. Knight recognizes this, otherwise he would not be a psychoanalyst. I wonder whether we are not too glib in talking of the reality situation of our patients or at any rate using it in a definition as does Dr. Strecker, who was quoted by Dr. Ebaugh. The dynamic problems do not permit me, at any rate, to claim for any one static reality situation such importance that it is differential. The chronic alcoholic addicts in their maladjustments that are brought to the morals court I find can best be approached and only approached by a modified psychoanalytic technic. I have been surprised how easy it is to give and how eager most of these patients are to obtain an understanding of themselves. So many

of them are with female dominance in the picture or impotent or have homosexual tendencies that the approach is not difficult. And the results have been fairly satisfactory—more so than in the class that Dr. Knight discussed, in which I have only a long record of disappointments. Dr. Knight, more skilled in psychoanalytic technic, can get better results, as his paper indicates, than the average social psychiatrist. His effort and his results deserve commendation.

DR. HERMAN S. MAJOR, Kansas City, Mo.: The method of treatment of alcoholic addiction in the clinic with which I am affiliated differs somewhat from the treatment presented by Dr. Knight in that we give patients liquor for a period of two or three days if they are drinking when they come in. We recognize that alcohol is not only a poison but a narcotic and that alcoholism is a disease and not a habit. There are five things that we attempt to do with our patients. We eliminate the poison from the system, we remove the desire for liquor, and we build up the patients' nervous systems and build them up physically, and then we attempt to change their psychologic outlook in that we endeavor to impress on them the fact that it is not the taint that does the damage but it is the person; therefore, regardless of what other people may do, they must adopt the psychologic view that as far as they are concerned they are too smart and they have too much sense to take poison and a narcotic deliberately into their systems. We do not restrain our patients and we refuse to accept restraint cases. Our patients are permitted to go out without being accompanied by an attendant forty-eight hours after they have taken their last drink of liquor. They are permitted to go out the first day for one hour in the forenoon and one hour in the afternoon, the next day for two hours in the forenoon and two hours in the afternoon, and following that they can take their medicine with them and go to a picture show or elsewhere without supervision. We have only one patient out of every 500 who betrays our confidence by getting something to drink while he is on the outside. We do not think that it is fair to punish 499 others just to catch one fellow who does not want to do the right thing. We lecture to our patients on the effects of alcoholism on the nervous system. We have had experience with several thousand cases, and out of every hundred patients who remain with us for four weeks with the follow-up treatment at home and subsequent check-up, eighty remain abstinent. Of the fifteen or twenty who resort to drinking we find that they do so not because they have a desire for drinking but because they want to be good fellows, and a good many of them return and take the treatment a second time. They have learned their mistake and most of them make good. I think the psychologic treatment after one has had the alcohol eliminated from the patient is an important measure.

DR. ROBERT P. KNIGHT, Topeka, Kan.: Dr. Ebaugh's classification of drinking coincides closely with mine. His "situational" group is practically equivalent to the "reactive" group of which I spoke, the "simplex" group is equivalent to my "essential" group, and the symptomatic cases, which comprised my third division, include his psychopaths, psychotics and neurotics. I agree with him that a sociologic study is necessary, and I would call attention to a good suggestion made by newspaper columnist Westbrook Pegler to the effect that the liquor industry be taxed and the proceeds used to pay for the treatment of those who overuse their products. This is an excellent idea. With Dr. Menninger's remarks I agree. With regard to Dr. Mayer's comments, I do not believe that we need to be vague about what "reality" is. If an alcoholic addict has a dominating wife, if he has children and cannot endure their being taken care of in the way that he wants to be taken care of and cannot admit, if his father has recently died and he was always dependent on his father for financial support, these are factors in his reality. With regard to Dr. Mayer's point about impotence sustaining the alcoholism, I would look on both the impotence and the alcoholism as symptoms. The impotence often precedes the alcoholism, and while it may be true that the one now sustains the other, one may not list these as cause and effect. With regard to Dr. Major's remarks, persuasion and lecturing of alcoholic addicts has been going on for many years. The relatives and the preacher try it long before they consult

the psychiatrist. The alcoholic addict knows that he is taking a poison into his system. If one uses this approach to try to persuade him not to drink, one is neglecting entirely the point that many alcoholic addicts drink because they unconsciously want to destroy themselves from strong feelings of guilt and need for self punishment. With regard to Dr. Major's remarks about eighty alcoholic addicts out of every hundred treated remaining abstinent, congratulations!

CEREBROCRANIAL INJURIES

DETAILED STUDY OF 1,433 CASES

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The past quarter of a century has witnessed an increase in the number of cerebrocranial injuries in both the larger centers and the rural districts throughout the land. What was at the beginning of this century a rare surgical problem has become one of frequent occurrence in hospital practice. The American Medical Association and the American College of Surgeons have both given it wide publicity, and scientific statistical exhibits on this subject have been displayed at their annual meetings; state societies and regional meetings have featured papers on it; journals have published excellent articles covering all phases of the subject;

TABLE 1.—Mortality Study in Seattle Over a Period of Eighteen Years

Period	No. of Cases	Death Within 3 Hr.	Death Within 24 Hr.	Death After 24 Hr.	Total Mortality
1919-1924..... 60 months	178	60.7%
March 1931-December 1932..... 21 months	175	23.3%
October 1933-March 1935..... 6 months	214	19.1%
October 1936-March 1937..... 6 months	145	..	10 66%	5 33%	15 10.3%
October 1937-December 1937..... 3 months	107	4 30%	10 77%	3 23%	13 12.1%

research workers have contributed their share, and hospitals have furnished equipment and supplies desired by surgeons in the treatment of these patients. The result of all these combined efforts has been to decrease the mortality; nevertheless the incidence has rapidly increased (table 1).

Recent articles have shown remarkable agreement in the basic factors involved in handling any serious cerebrocranial injury.¹ The reports of series studied in various centers have shown a tendency toward uniformity in treatment and results obtained. A striking fact in these reports is that with each series from large centers the percentage of operative intervention has shown a gradual decline; a standardized technic for the emergency treatment has been adopted. In this emergency treatment great importance is attached to maintenance of water balance; measures to relieve or prevent shock are considered as imperative first aid essentials; delayed roentgenography is advisable except in com-

pound comminuted fractures, and, finally, patients are given more or less standardized treatment for twenty-four hours. Of the patients who have survived the acute stage, those with mild injuries are given simple rest and those with severe injuries are transferred to the care of more experienced surgeons and nurses for expert post-traumatic attention.

From time to time we have made reports on our results obtained during the past fifteen years.² We have had demonstrations at various county, state and regional medical meetings. At Harborview (King County Hospital)³ we have adopted a uniform or standard treatment based on our observation of results obtained. This has been changed from time to time as we have become convinced that certain forms of treatment give better results. The occasional spinal puncture, for instance, has in our service become established as routine on all patients who survive the first twenty-four hour period. Spinal drainage repeated daily on all patients who show blood in the first puncture is continued until the fluid returns clear. Encephalography in all patients having a persistent severe headache with a spinal fluid manometric measurement above 6 mm. of mercury in the prone position is considered advisable for both diagnostic (blood clot) and therapeutic purposes. Under this routine our morbidity has been lessened and our mortality has been decreased almost 50 per cent (table 2).

The first treatment has been directed toward the control of shock. Absolutely no other objective is considered. This may require only a few hours or may take a longer period. The treatment aims to keep the water volume in the vascular system, carry oxygen to the brain cells, prevent accumulation of fluid in the interstitial spaces and support the heart.

Our routine regarding spinal punctures is as follows: Every patient who has shown definite signs of concussion or skull fracture or concussion and skull fracture combined is given a spinal puncture after the first twenty-four hours and before leaving the hospital. Certain patients may have spinal punctures before this period. In mild cases spinal punctures are usually performed about the twelfth hour. In serious cases, spinal punctures should be delayed until after the small veins have thrombosed or the arteries have contracted. This will prevent a recurrence of hemorrhage from these vessels. Since we have adopted the rule, we have been able to segregate our patients and hold many in the hospital who might otherwise have been permitted to go home or be transferred to another hospital. The presence of bloody cerebrospinal fluid in our experience immediately stamps the case as one with at least a mortality rating of 45 per cent. We have not felt that withdrawal of 5 or 10 cc. of fluid in the prone position adds any risk to the patient. We have not seen bad effects in a single case. Many patients have been greatly benefited. Spinal punctures were done on 121 in one series of 145 patients and on fifty in a series of 169 patients. In the first series of 121 cases bloody spinal fluid was found in forty-one cases, while it was

Read before the Section on Surgery, General and Abdominal, at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 15, 1938.

1. Munro, Donald: The Emergency Care of Cerebrocranial Injuries, *Am. J. Surg.* 38: 739-744 (Dec.) 1937. Gotten, Nicholas: Head Trauma, *J. A. M. A.* 110: 1727-1730 (May 21) 1938.

2. Swift, G. W.: Cerebral Injuries Due to External Trauma, *Surg., Gynec. & Obst.* 62: 340-346 (Feb. 15) 1936; Head Injuries, *Am. J. Surg.* 21: 152-158 (Oct.) 1934; Cerebrocranial Injuries, *West. J. Surg., Obst. & Gynec.* 40: 343-354 (July) 1932; Head Injuries of Moderate Degree, *Northwest Med.* 30: 16 (Jan.) 1931. Berens, S. N.: Head Injuries, *West. J. Surg., Obst. & Gynec.* 44: 624-635 (Nov.) 1936; Cerebrocranial Injuries, *Harborview Bull.* 1: 10-14 (Feb.) 1933; Moderate and Severe Cerebrocranial Injuries, *S. Clin. North America* 13: 1277-1281 (Dec.) 1933; Summary of Eighty-Six Cases of Cerebrocranial Injuries, *West. J. Surg., Obst. & Gynec.* 40: 409-415 (Aug.) 1932.

3. King County Hospital is commonly known as Harborview Hospital.

found in twenty-five in the series of fifty cases. A total of 171 patients, or 54 per cent, of the total series had spinal punctures and of these sixty-six, or 21 per cent, of the total series had bloody spinal fluid.

Roentgenograms demonstrated fractures in fifteen, or 4 per cent, of the series. However, this is not so significant because none were taken until after the first forty-eight hours and, if the spinal fluid was free from blood and the patient recovered completely from shock, no roentgenograms were taken. It is not always possible to obtain films for one or another reason.

The question arose as to how the figures compared with the results in other hospitals. First we studied our series of 145 cases during a six months service at Harborview. Then we studied 169 cases during the following six months in the next service where the same treatment, except for routine spinal drainage, was used. We sent a questionnaire to all the standardized hospitals in the state of Washington, asking for a report on all their hospitalized cerebrocranial injuries treated during the same annual period. The purpose of the survey was to determine certain fundamental facts which we believe to be true. The Northwest has had a very intensive campaign for the past ten years directed toward a better understanding of the principles on which modern treatment of severe cerebrocranial injuries is based. Such national leaders as Fay,⁴ Mock,⁵ Adson,⁶ Craig⁷ and Ochsner⁸ have presented the subject before county and regional medical meetings. Practical demonstrations, tabulations of results, exhibits of scientific specimens, illustrations of various lesions and physiologic reactions of water balance have been presented at many meetings throughout the state of Washington. Interns who have had an intensive training have located in many smaller centers and have spread the knowledge gained at the large hospitals in the larger cities. It was our belief that if the fundamental principles were sound the state

(2) the reports from the state board of health were essentially identical, we knew that the mortality figures were accurate. We did find a lower mortality in our lists than in the official list because of the fact that in a certain percentage of fatal cases the patient never reaches the hospital but is taken directly to the morgue. These form a considerable number of the total and of course increase the total mortality for the city. Some hospitals do not consider a patient who dies within an hour or so

TABLE 3.—Mortality Study: Dr. Temple Fay, Philadelphia

	No. of Cases	Death Within 3 Hr.	Death After 3 Hr.	Total Deaths
1. Concussion only.....	342	3 0.8%	16 4.6%	19 5.4%
2. Skull fracture, clear spinal fluid....	53	4 7.5%	3 5.7%	7 13.2%
3. Blood in spinal fluid, concussion, no fracture	115	6 5.2%	24 20.8%	30 26%
4. Skull fracture, blood in spinal fluid, concussion	145	14 9.6%	47 32.4%	61 42%
Totals.....	655	27 4.1%	90 13.7%	117 17.8%

after admission as a hospital patient and make no record. Several such instances were found in our check-up.

In order to compare our records with others, we obtained a detailed report (table 3) from Dr. Temple Fay of the Temple University Hospital of Temple University School of Medicine, Philadelphia, of the results he obtained in his clinic. Fay has included in his series all the patients admitted to the Neurosurgical Department, even those who died within the period of an hour. In his report 4.1 per cent died within three hours. In our series 7 per cent died within twenty-four hours. Fay's final mortality is based on his entire series of head injuries. Perhaps his last hundred cases would show a much lower mortality. Also I have tabulated the results of a series of cases (table 4) by Dr. Harry E. Mock of St. Luke's Hospital and Northwestern University Medical School, Chicago. This includes a series of private patients and another series of proved skull fractures submitted to him by eighty surgeons throughout the country, showing the end results. Both Fay's and Mock's final mortality include all their cases reported during the last few years. Temple University Hospital is situated in the center of Philadelphia and undoubtedly receives many emergency cases presenting severe injuries. This would tend to increase the mortality in Fay's tabulations. St. Luke's Hospital is located in the center of Chicago, but according to Mock's tabulations 10 per cent of his patients died from concussion only while 5.4 per cent of Fay's patients died from concussion only. Possibly this accounts for the difference in their mortality rate. Harborview Hospital received all emergency cases until 1936, and our mortality was 19.1 per cent. Since then emergency cases are taken to the nearest hospital. This undoubtedly accounts for the rapid decrease in the mortality of Harborview Hospital.

In the series of 314 cases at Harborview there were thirty-seven deaths. Of these twenty-two, or 59.4 per cent, of the deaths occurred within twenty-four hours. Another four deaths occurred within the second twenty-four hour period, making 70 per cent of the total number of deaths within forty-eight hours. These deaths were not always due to the head injury alone. In some instances severe chest and abdominal injuries may have

TABLE 2.—Morbidity Study: Comparative Period of Hospitalization

	No. of Cases	Less Than 1 Week	1-2 Weeks	2+ Weeks
King County Hospital				
Series A.....	145	107 73%	28 19%	10 6.9%
Series B.....	169	130 77%	25 15%	14 8.3%
Total.....	314	237 75%	53 17%	24 7%
Other Seattle hospitals.....	222	144 65%	40 18%	38 17%
All hospitals in Washington.....	1,433	960 67%	249 17%	224 15%

of Washington should have a valuable report to submit in the care and treatment of cerebrocranial injuries.

In order to check the reports from an impartial angle, all deaths reported to the state of Washington from the cities of Seattle and Yakima were reviewed. As the two series (1) the questionnaires from the hospitals and

4. Fay, Temple: The Treatment of Acute and Chronic Cases of Cerebral Trauma by Method of Dehydration, *Ann. Surg.* 101: 76-132 (Jan.) 1935; Personal communication to the authors, 1937.
5. Mock, H. E.: Management of Skull Fractures, *New England J. Med.* 214: 625-634 (March 26) 1936; Personal communication to the authors, 1938.
6. Adson, A. W.: The Treatment of Injuries to the Head, *Internat. J. Med. & Surg.* 43: 617 (Dec.) 1930.
7. Craig, W. McK.; Adson, A. W.: Spontaneous Intracerebral Hemorrhage: Etiology and Surgical Treatment, with Report of Nine Cases, *Arch. Neurol. & Psychiat.* 35: 701 (April) 1936.
8. Ochsner, Alton: Diagnosis and Treatment of Acute Cerebrocranial Injuries: Part I, *Am. J. Surg.* 12: 222-242 (May) 1931; Part II, *ibid.* 12: 523-531 (June) 1931.

been associated, but we included in this series all severe head injuries treated by the department of neurosurgery.

In table 5 we have made a more detailed study. We have used as a control (series A) 145 patients treated at Harborview in our service over a period of six months. One hundred and sixty-nine patients (series B) were treated the following six months in two different services. This totals 314 patients at Harborview

COMMENT

From these studies certain fundamental facts are apparent:

Early Shock.—The first important fact is that every patient brought to the hospital with a severe head injury should be given routine treatment for shock and then watched for signs of hemorrhage. Fay has shown in many articles, and his report again conclusively demonstrates, the value of water balance in the treatment of shock in head injuries. It is as important to prevent secondary shock as to control primary shock. This can be done only through sustaining the water balance.

Hemorrhage.—Most cases of hemorrhage can be controlled, but massive hemorrhages on the one hand and undiagnosed hemorrhages of the middle meninges on the other cause many of the deaths. The first cannot be controlled, but the second should be diagnosed and treated surgically. Petechial hemorrhages within the ventricular walls and brain stem cause death in cases of severe concussion. These again are beyond the reach of treatment. In Fay's series they caused 5.4 per cent of the deaths. Our series shows about the same proportion.

Morbidity.—Our tabulation shows that in the control series at Harborview the first and second series were almost identical; 73 to 77 per cent were hospitalized less than a week. This series includes (1) those patients who died within the first forty-eight hours, (2) those whose spinal puncture revealed no blood in the spinal fluid, (3) those who recovered promptly from shock and (4) those with no other serious injury. The study shows that this percentage decreases in the Seattle hospitals to 65 per cent and in the state hospitals to

TABLE 4.—Mortality Study: Dr. Harry E. Mock, Chicago

	No. of Cases	Mortality
Concussion only.....	550	10.0%
Concussion and skull fracture.....	275	17.8%
Total.....	825	12.7%
Cases reported to Dr. Mock by 80 surgeons		
Proved skull fracture.....	875	26%
Other cases reviewed.....	2,200	33%
Deaths within 24 hours.....		45%

for a period of one year. During this time the other hospitals in Seattle treated 222 cases. We tabulated the cases treated in hospitals in the state of Washington with 100 or more cases, those with from twenty to 100 and those with less than twenty cases. We then compared the results in 1,433 cases treated in all the hospitals in Washington.

We studied the total number of deaths in the hospitals with more than 100 cases, with twenty to 100 cases and with less than twenty cases and compared the number of deaths which occurred between twenty-four and forty-eight hours and after forty-eight hours (table 7). In this study it is interesting to note that 55 per cent of the deaths occurred within the first twenty-four hours

TABLE 5.—Comparative Mortality: 1,433 Cerebrocranial Injuries—Oct. 1, 1936, to Oct. 1, 1937

	Total No. of Cases	Positive Signs of Skull or Brain Injury	Other Serious Injuries	Spinal Punctures	Spinal Drainage	Intra-cranial Operations	Deaths After Operations	Operative Mortality in Total Cases	Deaths Within 24 Hr.	Deaths Within 48 Hr.	Total Deaths	Mortality Percentage
King County Hospital												
Series A.....	145	105 72%	21 14%	121 83%	25 17%	0	0	0	10 7%	1 0.7%	15	10.3%
Series B.....	169	132 78%	27 16%	50 30%	17 10%	0	0	0	12 7%	3 1.8%	22	13.0%
Total King County Hospital...	314	237 75%	48 15%	171 54%	42 12%	0	0	0	22 7%	4 1.2%	37	11.7%
Other Seattle hospitals.....	222	153 70%	24 10%	40 18%	10 5%	14 6.3%	5 30%	2.2%	14 6.3%	4 1.5%	29	13.0%
Hospitals with 100+ cases.....	704	48%	16%	27%	6%	0.6%	50%	0.28%	6%	1.1%	84	12.0%
Hospitals with 20-100 cases.....	560	48%	14%	13%	3.4%	2.8%	31%	0.89%	9%	2%	94	17.0%
Hospitals with 20 cases or less.....	169	50%	15%	24%	5%	5.9%	20%	1.1%	5%	1.1%	17	10.0%
All hospitals in Washington.....	1,433	49%	15%	21%	6%	2%	30%	0.68%	7%	1.7%	195	13.6%

and in an additional 13 per cent death occurred within the next twenty-four hours; in almost 70 per cent death occurred within the first forty-eight hours.

Finally we made a study of the morbidity in Harborview (series A and B), other hospitals in Seattle, and all the hospitals in the state of Washington (table 6). It is interesting to note that in series A 73 per cent of the patients remained in the hospital less than a week, 19 per cent remained less than two weeks and 6.9 per cent remained more than two weeks. In series B 8.3 per cent remained in the hospital more than two weeks. The only difference between series A and series B was the spinal drainage. We believe that this accounts for the lower morbidity.

67 per cent. In other words, under the assumption that the treatment is the same, except for a decrease in the number of spinal taps for diagnostic purposes, if the number of patients leaving the hospital is greater owing to the positive assurance of absence of severe injury obtained from taps (clear spinal fluid) the treatment is well worth while. In the next column—those remaining less than two weeks—it is found that all series show 17 per cent average, except the controls at Harborview, where the percentage is 19 per cent. Here the difference is in spinal drainage, and in the series in which drainage is routine for patients with bloody spinal fluid and a careful check on water balance is maintained, the percentage drops from 19 to 15. This should also

show in the lessened morbidity, the stay in the hospital being prolonged beyond the two weeks period: Harborview control 6.9 per cent; other services 8.3 per cent; average 7 per cent; Seattle hospitals 17 per cent; state hospitals 15 per cent. The conclusion must be that spinal drainage and water balance control lower the morbidity and decrease the hospital period.

Special Treatment.—The study gives a further suggestion regarding treatment. In the larger hospitals where more attention can be given both by the hospital personnel and by the surgeon specially trained to treat these patients, one finds a lower mortality and morbidity and better end results; the records are better kept and the combined results are better. In the smaller hospitals, again, these same factors are present. Usually one surgeon sees all the patients and he becomes expert in handling them. He equips himself to meet emergencies; he calls in outside help whenever he finds a serious factor developing. He uses the long distance telephone to secure expert consultation, and his records show a better result. In the larger private hospitals more individual surgeons treat a small number of

4. Every hospital should have at least one surgeon on its staff who makes a special study of this type of case and is available for consultation in regard to all serious complications.

5. Spinal puncture and spinal drainage, water balance control and constant care should be used in an effort to save lives, classify cases, prevent morbidity, and shorten hospitalization.

6. Records should be kept so that any subsequent study of the cases may be of some value.

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ABSTRACT OF DISCUSSION

DR. HARRY E. MOCK, Chicago: The Pacific Northwest, and especially the state of Washington, have become head-injury conscious. As a result, the high mortality from this type of trauma has been definitely lowered. My opinion has been that the statistical study of mortality rates for purposes of comparison should be based on some common measuring rod. One man's interpretation of the seriousness of a head injury may differ widely from another's. Thus, in comparing my mortality rate in 275 proved skull fractures with approximately 3,000 proved skull fractures collected from other sources, I have used the presence of a skull fracture as the common measuring rod. Since the presence of the fracture adds materially to the seriousness in the majority of cases, the mortality rate in proved skull fractures is bound to be higher than in a group including all head injuries, regardless of fractures. The serious head injury requires exactly the same meticulous management as does the skull fracture. Since from 50 to 60 per cent of the deaths from skull fracture occur in the first twenty-four hours, and since the majority of these cases occur outside the medical centers where neurosurgeons reside, it is evident that the emergency and early management of these cases falls largely to the general physicians and surgeons throughout the country. This will always be a social problem the solution of which is the responsibility of the rank and file of the profession as well as of the specialist. There is no routine treatment applicable in every cerebrocranial injury. The treatment adopted depends absolutely on the signs and symptoms of each individual case. In the more serious brain injuries these signs and symptoms, indicating increasing cerebral volume, increasing intracranial pressure and threatened medullary compression, develop and change rapidly in character during the first twenty-four hours. It is essential, therefore, that an hourly chart of the pulse, respiration, blood pressure and often the temperature be kept and frequently studied, that the attending surgeon practically live with such patients, if these changes are to be noted in time to institute the indicated life-saving procedures. Speaking in terms of skull fracture, the high mortality rate can be reduced. Many will be saved if heed is given to the authors' remarks concerning shock. Based solely on their signs and symptoms, dehydration will meet the situation in approximately 50 per cent of the cases. It should never be carried to the absurd point of overdehydration. Spinal puncture, definitely indicated in approximately 34 per cent of all skull fractures, is the greatest life-saving measure.

DR. GEORGE W. SWIFT, Seattle: Dr. Mock and I do not agree on what the measuring rod should be, but it does not matter how one arrives at statistics if one keeps reporting from time to time and uses the same measuring rod for his report. That is what I have tried to do and I am sure that is what Dr. Mock has done. In the end, if we tabulate our records, we all come within a few points. Dr. Temple Fay has practically the same mortality rate as we have as shown by his tabulation. Dr. Mock mentioned the incidence of operative intervention as being approximately 5 per cent in his series. It is lower in our series. Dr. Dandy, on the other hand, has higher incidences. We are all attempting to arrive at the same general end results in the method that each of us prefers to use. Dr. Dandy is one of America's most skillful neurosurgeons. In his hands, operative procedures are easy and undoubtedly save many lives. For the rank and file of surgeons in America to have his keenness of operative sense and operative ability is hardly possible. They must have other means at their command

TABLE 6.—Mortality Study

Total Deaths	Within 24 Hr.	24 to 48 Hr.	After 48 Hr.
Hospitals with 100+ cases (84 deaths).....	45 53.5%	8 10%	31 36.5%
Hospitals with 20-100 cases (94 deaths).....	53 56.4%	15 16%	26 27.6%
Hospitals with 20 cases or less (17 deaths).....	10 58.8%	2 12%	5 27.2%
Totals (195 deaths).....	108 55.4%	25 13%	62 31.6%

patients; frequently there is no intern or the intern is too occupied with many other duties to give his undivided attention to the individual case; no routine has been established for the emergency treatment in all cases and the result is shown in the records: a greater morbidity and a higher mortality. A further factor which one must consider in this relation is that private hospitals receive patients with severe head injuries in emergencies. When identification has been completed and the shock symptoms have subsided, the indigent patients are transferred to the county hospitals. These are the poorly nourished, older and possibly diseased patients; facts which tend to increase the percentage at the county hospitals. Again in the county emergency hospitals after the identification has been completed and shock symptoms have subsided, many patients able to pay for private care are transferred to other hospitals. This tends to increase the percentage of the first week hospital period in the county hospitals and to increase the percentage of the lower hospital periods in the private hospital group. These conditions would suggest that the private hospitals should have much better results than the county or smaller hospitals, but the records do not substantiate this.

CONCLUSIONS

1. Periodic statistical studies should be made by each hospital caring for severe head injuries.

2. The average percentage established for the region by the county hospital should represent at least the lowest figure with which the hospital staff should be satisfied.

3. Special emergency routine care should be established and insisted on from any and all surgeons.

to reach the same end. In the hands of Dr. Fay, dehydration is the ideal treatment. Perhaps no man in America can handle a head injury case with such skill in the use of water balance. He uses dehydration for the same end result as does Dr. Dandy: the operative release of the encased fluid in the subdural and subarachnoid spaces. Here again the exercise of proper skill and judgment in the maintenance of water balance requires exceptional ability. We attempt to obtain the same results by spinal drainage. We feel that the average surgeon throughout the country had better rely on this very simple procedure rather than the more difficult surgical intervention and more technical water balance maintenance. In the end, what we all try to do is to prevent an accumulation of fluid, blood or spinal fluid within the cranial cavity to such a degree as to stop the normal function of the brain.

MEDICAL SUPERVISION OF BENZENE PLANT WORKERS

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The current emphasis on preventive efforts in medical practice finds its counterpart in the rapidly progressing field of industrial medicine. The medical departments of mills and factories, at first concerned only with the repair of injuries caused by accidents, later devoted time to the diagnosis and treatment of disabling occupational diseases. The time is at hand when plant physicians must extend their interests beyond the walls of their offices and cooperate with engineers in the eradication of industrial disease at the points of its inception. The industrial physician's essential part in this program is one of constant supervision over the physical status of workers. When workers handle toxic substances, even though they are afforded theoretically perfect mechanical protection, the medical surveillance must be methodical and unremitting. This rule holds for the supervision of benzene (benzol, C_6H_6) plant workers, who are usually considered to be free from the danger of chronic benzene poisoning.

At the time the work reported here was begun it was felt that a satisfactory supervision of such workers should include three procedures: (1) the periodic determination of the relative proportions of inorganic and organic sulfate in the urine of employees, as first suggested by Yant and his co-workers¹ and later advocated by Schrenk and his associates;² (2) complete hematologic studies of the workers, and (3) determination of the concentration of benzene in the air at various points in the workings.

The plant for which this study was made regularly employed about eighteen men, whose ages when first examined varied from 20 to 53 years and whose work exposure ranged from twelve months to fifteen consecutive years. The project was begun in August 1936, with complete physical, hematologic and urinary

examinations of each employee. Urine sulfates were determined as a part of this examination. Thereafter they were determined once each month, and the blood was examined about every six months. Determinations of the concentration of benzene in the air of the plant were made at irregular intervals and then chiefly for the purpose of checking the satisfactory operation of the ventilating equipment as well as the information gained by clinical methods.

URINE SULFATES

Preliminary Considerations and Studies.—The value of the inorganic-organic sulfate ratio in the urine as a factor indicating benzene absorption was first established by the workers headed by Yant¹ at the Pittsburgh station of the U. S. Bureau of Mines. It was shown by them that the absorption of even small amounts of benzene causes an increased proportion of the total sulfates of the urine to appear as organic salts. The explanation offered for this phenomenon was that the absorbed benzene is oxidized in the body to phenolic products, which are conjugated with sulfates by the liver and eliminated as such combinations by the kidneys. This explanation is well supported by previous work, quoted by Kahn and Goodridge.³ It was theorized that severe damage to the liver would interfere with this normal process of detoxification, and Smyth⁴ found that persistently high levels of inorganic urine sulfates obtained in animals subjected to toxic concentrations of carbon tetrachloride.

Yant's experiments, performed on dogs, showed that of the total sulfate of the urine from 10 to 15 per cent ordinarily is present in organic form and that the remaining 85 to 90 per cent occurs as inorganic salts. Animals exposed to 100 parts per million of benzene in air (the concentration generally accepted as being non-toxic for man) for eight hours showed a definite shift in favor of the organic component of the total urine sulfates. With increased concentrations of benzene in the air and greater exposure times the proportion of inorganic sulfates dropped rapidly and markedly. This characteristic reaction was found to precede changes in the blood by considerable periods, occasionally by many months. In a subsequent publication the same group⁵ reported that the proportion of inorganic sulfate in the urine of healthy, unexposed men might occasionally drop to 81 per cent of the total sulfates eliminated.

A total of 106 specimens of urine from a like number of normal, unexposed workers were examined as controls to one phase or another of the present study. Five showed a value for inorganic sulfate in the range from 77.08 per cent (the lowest encountered among unexposed normal persons) to 80 per cent of the total sulfate. In all the remaining 101 specimens the inorganic fraction was greater than 80 per cent of the total sulfate.

Efforts at establishing a satisfactory technic showed that specimens of urine could be stored at 45 F. for at least two weeks without altering the sulfate ratio. A trial of the several methods described in standard textbooks⁶ for determining sulfates in urine showed that in the laboratory in which this work was to be done the

Read before the Section on Preventive and Industrial Medicine and Public Health at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 15, 1938.

1. Yant, W. P.; Schrenk, H. H.; Horvath, A. A., and Reinhart, W. H.: Urine Sulfate Determinations as a Measure of Benzene Exposure. *J. Indust. Hyg. & Toxicol.* 18: 69 (Jan.) 1936.

2. Schrenk, H. H.; Yant, W. P., and Sayers, R. R.: A New Procedure for the Control of Benzene Exposure. *J. A. M. A.* 107: 849 (Sept. 12) 1936.

3. Kahn, Max, and Goodridge, F. G.: Sulfur Metabolism: A Review of the Literature, Philadelphia, Lea & Febiger, 1926, p. 529.

4. Smyth, H. F., in discussion on Schrenk, Yant and Sayers.

5. Peters, J. P., and Van Slyke, D. D.: Quantitative Clinical Chemistry, Baltimore, Williams & Wilkins Company, 1932, vol. 2, p. 892.

6. Morse, Withrow, and Looney, J. M.: Applied Biochemistry, ed. 2, Philadelphia, W. B. Saunders Company, 1927, p. 794. Hawk, P. B., and Bergheim, Olaf: Practical Physiological Chemistry, Philadelphia, P. Blakiston's Son & Co., 1927, p. 770. Mathews, A. P.: Physiological Chemistry, New York, William Wood & Co., 1924, p. 1105.

method of Folin⁶ was the most satisfactory from the standpoint of ease of performance and duplication of results. This also was the method used in the original work at the Bureau of Mines.¹

An attempt was made to determine the diagnostic specificity of a drop in percentage of inorganic urine sulfates. An arrangement was made with a local hospital whereby specimens of urine from patients with proved diagnoses could be examined. The specimens were stored in a refrigerator immediately on collection and were analyzed within a few days. An opportunity presented itself at the same time for studying the effect on urine sulfates of drugs containing benzene radicals in their chemical structure.

The urine of 108 hospital patients was examined. It developed that this portion of the study could not be satisfactorily controlled, and definite conclusions can therefore not be drawn. Two of the patients were being treated for acute rheumatic fever. The first of these was receiving 30 grains (2 Gm.) of sodium salicylate daily, and the second was receiving 60 grains (4 Gm.) daily of the same drug. The inorganic fraction of the total sulfate was 64.29 and 68.08 per cent, respectively. No specific condition was encountered which of itself, independently of medication, caused a significant shift in the sulfate ratio. Nonbenzene workers under treatment for syphilis and receiving one or two injections of neoarsphenamine or mapharsen weekly showed no decrease in inorganic sulfates below 80 per cent of total urine sulfate.

Studies on Benzene Plant Workers.—It was pointed out by Yant¹ that the elimination of benzene is greatest when its absorption is at its peak and that with the cessation of exposure elimination drops off progressively with the passage of time. In order to insure the obtaining of urine from workers during their periods of greatest exposure, appointments for their appearance at the clinical laboratory for the purpose of voiding specimens were carefully worked out. Each man reported during his shift and only after he had worked for three successive days. The specimens were stored in an electric refrigerator until they could be conveniently analyzed, usually from one to four days later. They were voided in the presence of a technician and analyzed by a chemist's assistant whose ordinary work it was to make quantitative chemical analyses in the coke plant a short distance away. Specimens were sent to him with only a number for identification.

As was previously stated, specimens were usually analyzed for each worker every month during the period of this study. The average number of men employed during the eighteen months covered was eighteen. A total of 240 sulfate determinations was made on single specimens of urine. The lowest value for inorganic sulfate revealed by these examinations was 66.34 per cent of the total sulfate. The inorganic fraction of the total sulfates ranged from this figure to 70 per cent in two instances, from 70 to 80 per cent in twenty-eight instances and above 80 per cent for the remaining 210 analyses. Readings below 80 per cent occurred thirty times for ten men.

HEMATOLOGIC STUDIES

Hamilton⁷ has stressed the importance of making complete blood counts for patients suspected of having

chronic benzene poisoning and has condemned the practice of expecting a so-called typical picture. She expressed the opinion that there may be destruction of any of the cellular components of the blood. That neutropenia commonly follows overdoses of benzene by alimentary or respiratory portals is well recognized. Duke⁸ reported experimental work showing that the platelet count may be reduced. Hayhurst and Neiswander⁹ reported a case in which, among other significant abnormalities, there was increased fragility of

Summary of Urine Sulfate Values for Workers Showing Secondary Anemia

Case	Date	Inorganic Sulfate, Percentage	Red Blood Cells, Millions per C. Mm.	Hemoglobin, Gm.
1.....	8/26/36 12/18/36 1/ 8/37 7/13/37 8/ 9/37 11/13/37 1/ 5/38	82.50 74.02 77.33 83.02 83.33 70.75 67.74	4.30 3.81 4.08 4.34	14.0 12.0 13.5 14.0
2.....	11/27/36 12/18/36 1/27/37	88.25 87.88 87.60	3.40 4.57	13.5 14.0
3.....	7/29/37 8/13/37	84.61 84.93	4.21	14.0
4.....	12/14/36 1/ 8/37 11/ 9/37 1/ 6/38	96.37 91.78 78.31 78.57	4.10 4.02	14.5 15.0
5.....	7/29/37 8/19/37	87.68 88.40	4.12	14.0
6.....	7/13/37 8/ 9/37	84.01 88.03	4.31	14.5
7.....	8/28/36 11/ 9/37 1/ 5/38	94.03 90.07 87.93	4.32 4.29	14.0 14.5
8.....	8/27/36 7/28/37 8/19/37 11/ 9/37 12/31/37	93.86 94.44 93.62 87.00	4.05 4.25 4.15	13.0 14.0 14.0
9.....	7/13/37 8/23/37	91.31 84.59	4.30	14.0
10.....	7/29/37 8/ 9/37 11/16/37 1/ 4/38	88.98 88.06 88.39 86.24	4.12 4.35	14.0 14.0
11.....	9/27/37 12/31/37	91.89 90.54	4.28	14.0
12.....	8/28/36 7/13/37 8/ 6/37 11/ 9/37 1/ 7/38	96.08 82.16 89.13 77.78 93.33	4.10 3.74 4.14	14.0 13.5 15.0
13.....	7/29/37 8/19/37 11/ 9/37 12/30/37	74.22 81.90 73.91 71.34	4.21 4.24	15.5 15.0
14.....	7/12/37 8/ 4/37 12/29/37	91.12 83.48 80.33	4.30 4.06	15.0 13.0

the red blood corpuscles. Hurwitz and Drinker¹⁰ called attention to a possible impairment of prothrombin formation, and Hektoen¹¹ reported experiments showing that there is a decreased resistance to infection in animals receiving benzene by subcutaneous injections. An estimation of changes of the last two types was considered too difficult of achievement to be incorporated

8. Duke, W. W.: Causes of Variation in the Platelet Count, *Arch. Int. Med.* **11**:100 (Jan.) 1913.

9. Hayhurst, E. R., and Neiswander, B. E.: A Case of Chronic Benzene Poisoning, *J. A. M. A.* **96**:269 (Jan. 24) 1931.

10. Hurwitz, S. H., and Drinker, C. K.: The Factors of Coagulation in the Experimental Aplastic Anemia of Benzol Poisoning, with Special Reference to the Origin of Prothrombin, *J. Exper. Med.* **21**:400, 1915.

11. Hektoen, Ludwig: The Effect of Benzol on the Production of Antibodies, *J. Infect. Dis.* **19**:69, 1916.

6. Folin, Otto: On Sulfate and Sulfur Determinations, *J. Biol. Chem.* **1**:131, 1905-1906.

7. Hamilton, Alice: Industrial Toxicology, New York, Harper & Brothers, 1934, p. 156.

in the work being reported here. Besides this, the work of Hurwitz and Drinker showed that circulating prothrombin is diminished only with the advent of severe poisoning. No cases of this type were encountered in the present study.

The following were determined for each worker at the time of his first examination, in August 1936, and thereafter approximately at six month intervals: erythrocytes, leukocytes and platelets per cubic millimeter; differential white blood cell count; hemoglobin percentage, and fragility of the erythrocytes. Single determinations of the bleeding time and clotting time were made for each man. The sedimentation rate and the Kahn reaction of the blood were determined, and a complete urinalysis was performed at the first visit as a part of the general examination made of all employees of the firm.

If one considers the lower limit of normal for the erythrocyte count to be 4,500,000 per cubic millimeter, there were twenty-six subnormal counts for fourteen men. The accompanying table summarizes these and indicates where possible the figures representing the inorganic fraction of the total urine sulfates, both for the day of each blood count and for the preceding month. No abnormal total or differential white cell counts were noted in the entire study, and no increase in the fragility of the red blood corpuscles was encountered. Bleeding and clotting times, of which there were single determinations made for each worker, were all normal. There were no instances of thrombopenia.

BENZENE CONCENTRATION IN PLANT AIR

Determinations of the benzene concentration in the air were made according to the method of Schrenk and his co-workers.¹² As previously noted, they were not made with any planned regularity, and they were used chiefly to estimate the efficiency of ventilation. Determinations were made at all places revealed by plant inspection and clinical data on workmen to be points of possible benzene exposure.

For the most part the clinical data did not coincide with the results of air analyses. The explanation for this appears in the original articles of Schrenk and Yant. Air analyses determine concentrations at particular times and do not necessarily reflect conditions prevailing over long periods, whereas changes in the urine sulfate do indicate the degree of benzene exposure and absorption for a given employee's entire work day. When an employee's job takes him to a number of stations within the plant it becomes difficult indeed to estimate his exact exposure from air analyses alone. The difference in time between the obtaining of clinical data and the making of air determinations made impossible an exact correlation between the two in this study.

The highest concentration of benzene in the air found at any time was 400 parts per million. This was found at the only point in the plant where benzene cannot be kept entirely enclosed. Two workers (1 and 6 in the table) were presumably equally exposed at this job. The first (1) rather persistently showed an inorganic sulfate percentage of less than 80 and a lowered red blood cell count. The second (6) had only one subnormal red cell count and always had a normal urine sulfate ratio.

COMMENT

The experimental work of Schrenk and his associates has introduced a specific test for benzene exposure among workmen. When the inorganic fraction of the total urine sulfates of such persons drops markedly below the experimentally established normal of 80 per cent, there can be no doubt that benzene is being absorbed and excreted. Values ranging from 65 per cent to 80 per cent, however, represent a doubtful zone and are not to be used as specific evidence of benzene exposure. One needs to weigh other important factors, viz. the history of suspicious symptoms and exposure, the blood picture and the results of complete physical examination, before establishing the diagnosis of the milder forms of benzene morbidity. In a regular supervision of benzene plant workers one sees values for inorganic sulfate in the range from 70 per cent to 80 per cent of the total urine sulfate rather commonly interspersed throughout series of higher readings. From observations made on the present group of workers it can be stated that such values are not cause for concern.

Mild anemias, usually transitory, occur rather commonly among benzene plant workers, just as they do among most industrial workers. There were twenty-six red blood cell counts below 4,500,000 per cubic millimeter among fourteen men. Worker 1 had four such counts, of which two were associated with a value for inorganic urine sulfates above 80 per cent and two with values within the doubtful zone just below that figure. This worker, however, had enough other instances of a slightly lowered value for inorganic urine sulfate to warrant attributing his mild anemia to benzene inhalation. He had no other symptoms, such as anorexia, loss of weight or weakness.

The remaining lowered red blood cell counts observed in this study occurred in association with normal values for the inorganic urine sulfate. The exact causes for the slight anemia could not be discovered. That it was probably not serious was indicated by the further observation that within individual series the counts fluctuated between normal and subnormal figures from time to time, that none of the men lost weight, that absenteeism was about the average for the payroll of the entire firm and that the men always stated that they felt well.

Worker 2 had been employed about a month at the time of his first examination and worked at a point known to be nonhazardous. He had the lowest red cell count discovered in this study. His urine sulfate values confirmed the belief that he was absorbing no benzene and he was advised to have an obvious focus of infection treated. Two months later his red cell count had returned to normal and he had lost no time from his regular work. This case illustrates the advisability of hematologic studies on applicants for jobs which entail a possible benzene exposure.

The determination of the benzene content in the air of a plant has no great value as a routine measure in the supervision of the workmen's health. Significant concentrations are immediately detectable by the sense of smell, and careful inspection of plant equipment reveals their sources. The discovery of such concentrations properly falls to production foremen and workers. The detection of the smallest concentrations can more easily and certainly be accomplished by systematic determinations of urine sulfates among all exposed employees.

12. Schrenk, H. H.; Pearce, S. J., and Yant, W. P.: A Microcolorimetric Method for the Determination of Benzene, U. S. Department of the Interior, Bureau of Mines, report 3287.

CONCLUSIONS

1. The periodic determination of the inorganic fraction of the total sulfate in the urine of workers is an entirely satisfactory form of medical supervision of employees exposed to a possible benzene hazard. In plants where benzene is kept in closed containers a monthly examination of this type is adequate.

2. In the supervision of the workmen's health, hematologic studies find their chief practical value in the preemployment examinations of applicants for work.

3. In a given case of any blood dyscrasia in a worker in a plant using benzene, that substance should not be incriminated as the causative factor without a complete study of the worker and his job. A determination of the urine sulfate is helpful only if the subject is still at work and subjected to his customary exposure.

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ABSTRACT OF DISCUSSION

DR. PETER K. KNOEFEL, Louisville, Ky.: Benzene is changed in the body into phenolic substances, but since varying amounts of different phenols are formed and conjugated in different ways with sulfuric acid, with glycuronic acid, it may be seen how complex the quantitative aspect of the situation can be. Some factors which can influence the partition of urinary sulfate are known to be important. The condition of the liver which conjugates the phenols, and of the kidney which excretes them, certainly is important. The availability of sulfate in the body is probably less important. Little is known about the role of the diet and the presence of intestinal stasis. The Bureau of Mines group set an arbitrary level of 80 per cent of inorganic sulfate, figures below those indicating exposure to benzene. This is probably unjustified. Scott and Hastings in a large series of workers in various industries found cases of inorganic sulfate below 70 per cent, where there was no question of exposure to benzene, but what is needed is an even larger series of cases to establish the frequency of occurrence of any partition of urinary sulfate, so that in the end the probability of the chance occurrence of any fraction of sulfate can be expressed. In spite of all these difficulties, Dr. Kammer and his co-workers have shown what should be done to cope with such a situation.

DR. R. R. SAYERS, Washington, D. C.: I was glad to have the statements made by the authors, bringing out important points. One is that it is useful in the control of the exposure and that it is not a specific diagnostic procedure and is not intended as such; however, if, on examination of a group of workers by this method one finds that inorganic urinary sulfates are below 80 per cent of the total, it is time to see what control measures must be made; however, in some cases it will be found that the man had no exposure to benzene at any time. His condition may be due to something else entirely; but, if he is having exposure to benzene, the control measures can be corrected. The authors called attention to the point that just chemical analysis of the air are grab samples usually and do not indicate the efficiency of the control system; furthermore, if they did, the man is not in one spot at all times and he may be exposed to various quantities through the day, and it is the total exposure which is measured by the urinary sulfate method. The method should be further investigated. I think it may be useful.

DR. J. M. McCULLOUGH, Crockett, Calif.: I have used the white count in exposure and have found a definite drop in counts when a man was exposed within thirty-six hours of the time the count was taken. That count comes up within a week to ten days, but the exposure would stop. I can't give percentages, but occasionally where leaks have occurred the men would get enough to feel a certain amount of prostration. I have never had a case in which complete prostration occurred, but the men have complained of weakness and dizziness and some exhaustion, and the count was found down around 5,000. Where normal counts of from 8,000 to 10,000 had been observed,

they would drop to 5,000 and occasionally as low as 4,300. That comes up after five to seven days' time. I should like to hear from some one who has had the same experience.

DR. A. G. KAMMER, Indiana Harbor, East Chicago, Ind.: The only question raised in this discussion was the matter of white counts. We haven't seen a depression in the white counts. In case 1 the absorption found its expression in a lowered red count, and it is my opinion that a complete count would help more than just routine white counts.

RECENT STUDIES ON THE PATHO-
GENESIS OF WERLHOF'S
DISEASE

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AND

VITTORIO PUDDU, M.D.

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The relation between the spleen and the contents of platelets in circulating blood have for a long time now been admitted on purely clinical and empirical bases (therapeutic action of splenectomy in Werlhof's disease, thrombopenia secondary to primitive splenomegaly). Some series of researches carried out in the last few years seem to allow an experimental framing of this relationship and an interpretation of its nature.

In 1933 a series of researches on the subject was begun in the laboratory of this clinic. We¹ were able to establish that extracts of spleen taken from patients affected by Werlhof's disease applied in highly concentrated doses injure the megakaryocytes in cultures in vitro of the bone marrow of guinea pigs. The extraction was performed with the technic used in extracting trephones and therefore contained the whole hydrosoluble fraction dissolved, and the other fractions were suspended or in emulsion. So up to a point it could be called a total extract. From control researches carried on at the same time, it became evident that the normal spleen contains a similar principle, though less active, and later on that the same principle exists in the liver, lungs, red muscle, lymphatic glands and epiploon (Torrioli and Galeazzi,² Dimitrova³). Each normal organ and tissue proved on examination to possess a different degree of activity; according to the percentage of megakaryocytes injured in culture, they can be classed on a decreasing scale in the following order: epiploon, spleen, lymphatic gland, lung, liver, heart and red muscle. The hypothesis was advanced that these various degrees of activity were in proportion to the contents of the reticulo-endothelial tissue of the various organs and tissues examined.

In the meantime we⁴ were able to establish that, while the splenic artery blood serum was almost totally devoid of the toxic principle on the megakaryocytes, the splenic vein blood serum in subjects affected with Werlhof's disease contained this principle in high concentration. Torrioli and Pusic⁵ subsequently noticed

From the Medical Clinic (Prof. Cesare Frugoni) of the Regia Università degli Studi di Roma Facoltà di Medicina e Chirurgia.

1. Torrioli, Mario, and Puddu, Vittorio: Studi sulla biologia dei megacariociti sopravvivenuti in vitro: I. Tecnica; II. Azione di estratti di milza, Policlinico (sez. med.) 41: 245 (May) 1934.

2. Torrioli, Mario, and Galeazzi, M.: Studi sulla biologia dei megacariociti sopravvivenuti in vitro: III. Azione di estratti di muscolo e di fegato, Policlinico (sez. med.) 41: 647 (Nov.) 1934; IV. Azione di estratti di linfoghiandole, Boll. Soc. ital. biol. sperim. 10: 124 (Feb.) 1935.

3. Dimitrova, N.: Personal communication to the authors.

4. Torrioli, Mario, and Puddu, Vittorio: Studi sulla biologia dei megacariociti sopravvivenuti in vitro: V. Azione del sangue venoso splenico, Policlinico (sez. med.) 42: 129 (March) 1935.

5. Torrioli, Mario, and Pusic, G.: Azione piastrinopenica elettiva di dosi massive di estratto splenico, Boll. Soc. ital. biol. sperim. 9: 662 (Aug.) 1934.

that large doses of a protein-free aqueous extract of a normal spleen, injected intravenously into rabbits, strongly reduced the contents of platelets in their circulating blood. By varying, according to a given scale, the doses of extract in the culture of bone marrow, Torrioli and Belleli⁶ were ultimately able to prove that high doses injure the megakaryocytes while smaller doses not only do not injure them but, on the contrary, stimulate them, so that sometimes they assume an aspect similar to that which is considered as peculiar to the genesis of the platelets.

Taken as a whole, this set of researches seemed to point to a principle acting on the megakaryocytes, capable at high doses of injuring them and at reduced doses of stimulating them. This principle, elaborated by the principal reticulo-endothelial centers, seems to exceed normality in Werlhof's disease and to be likely to return to normality by means of splenectomy.

The results of researches quite recently carried out in the laboratories of Johns Hopkins Hospital in Baltimore appear to be in perfect unison with the ones already mentioned. By means of intravenous injections of a spleen digested extract from a patient with Werlhof's disease, Troland and Lee⁷ repeatedly obtained a strong diminution of the platelets in the circulating blood of rabbits. Troland and Lee seem to arrive at the conclusion that the thrombopenic substance is specific of the splenic tissue in Werlhof's disease. On this point, however, we wish to make a reservation. In the first place it should not be forgotten that a decrease of platelets in circulating blood was obtained by Torrioli and Pusic⁵ with normal spleen extract. In the second place the controls used by the American authors were thyroid tissue, myomatous uterus which, like muscular tissue, has almost no effect at all on the thrombopoietic system, and finally a spleen from a patient with Banti's disease and from one with hemolytic disorder, both of which differ widely from normal spleen as regards structural and functional plan. It is to be hoped that experiments with extracts of normal spleen and other normal organs will be made on a larger scale in order to set on a perfectly clear basis the point regarding the specific character of this principle, a point which appears to us of the utmost importance for the next step toward the future solution of the problem. We have mentioned the fact that this has already been done by Torrioli and Pusic,⁵ who, adopting for the extraction a technic of their own, have been led to results similar to those of Troland and Lee with the spleen in Werlhof's disease though on a smaller scale. Naturally it is also necessary to control in this same sense the extracts obtained with the technic of the Baltimore authors.

As to the chemical nature of the thrombopenic substance, we are obliged to admit that, at the present moment, we are unable to define it precisely. Neither our technic of extraction nor the technic of the American authors will allow any useful statement on this side of the question.

Via Genova, 24.

6. Torrioli, Mario, and Belleli, D.: Studi sulla biologia dei megacariociti sopravvissuti in vitro: VI. Azione di estratti di milza a concentrazioni scalari, Policlinico (sez. med.) 42: 214 (April) 1935.
7. Troland, C. E., and Lee, F. C.: A Preliminary Report on a Platelet-Reducing Substance in the Spleen of Thrombocytopenic Purpura, Bull. Johns Hopkins Hosp. 62: 85 (Jan.) 1938. The main article, Thrombocytopen: A Substance in the Extract from the Spleen of Patients with Idiopathic Thrombocytopenic Purpura that Reduces the Number of Blood Platelets, was published (J. A. M. A. 111: 221 [July 16] 1938) during the correction of the proof of this article.

SULFANILAMIDE EXCRETION IN HUMAN BREAST MILK

AND THE EFFECT ON BREAST-FED BABIES

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AND

J. P. PRATT, M.D.

DETROIT

Popularity of sulfanilamide in medical literature has created unusual interest and suggested broad therapeutic application. Originally introduced as a chemotherapeutic agent for the treatment of puerperal sepsis due to the beta hemolytic streptococcus, its value in that field has been repeatedly demonstrated. Many publications have emphasized the toxic effects on the patient from overdosage or on susceptible persons. On account of the frequent administration of sulfanilamide to nursing mothers, the following important questions are raised: 1. Is it excreted in breast milk? 2. If so, in what amounts? 3. What effect may be expected on the nursing babies? To answer these questions, quantitative estimations of free sulfanilamide were made on the blood and milk of nursing mothers and on the blood and urine of breast-fed babies.

The presence of sulfanilamide has been demonstrated in many body fluids and tissues. It is excreted chiefly

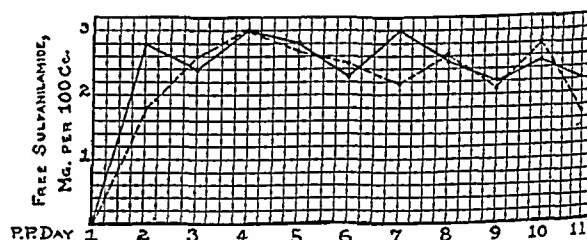


Chart 1.—Free sulfanilamide in the blood and milk of a mother on 60 grains (4 Gm.) of sulfanilamide daily. Blood indicated by solid line, milk by broken line. On a uniform dosage with normal renal function, the sulfanilamide concentrations in the blood and milk are closely parallel.

in the urine. Concentrations in the cerebrospinal fluid, pleural effusions, digestive juices, ascitic fluid and prostatic fluid are only slightly lower than in the blood stream. Marshall, Emerson and Cutting¹ have shown that in dogs sulfanilamide is present in all body tissues in approximately equal values, with the exception of bone and fat. From the investigations mentioned, one might infer that sulfanilamide is present in human breast milk. Quantitative studies were reported first by Hepburn, Paxson and Rogers² and recently by Adair, Hesseltine and Hac.³ Since toxic manifestations may occur during the administration of sulfanilamide, it is important to know in what concentration the drug is excreted in breast milk and the effect it has on the nursing baby.

METHOD

Twenty-eight normal convalescent women were studied during the first eight postpartum days. Only

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1. Marshall, E. K., Jr.; Emerson, Kendall, Jr., and Cutting, W. C.: The Distribution of Sulfanilamide in the Organism, J. Pharmacol. & Exper. Therap. 61: 196 (Oct.) 1937.
2. Hepburn, J. S.; Paxson, N. F., and Rogers, A. N.: Secretion of Ingested Sulfanilamide in Human Milk and in the Urine of the Infant, J. Biol. Chem. 123: liv (May) 1938.
3. Adair, F. L.; Hesseltine, H. C., and Hac, Lucile R.: An Experimental Study of the Behavior of Sulfanilamide, J. A. M. A. 111: 766 (Aug. 27) 1938.

those who secreted enough breast milk for adequate nursing were used. The technic of administration was based on the study of absorption and excretion of sulfanilamide as reported by Marshall, Emerson and Cutting,⁴ who found absorption complete in man in four hours after oral administration. The cases were divided into two groups according to dosage: Ten cases in group 1 received a daily total of 30 grains (2 Gm.) administered in doses of 5 grains (0.3 Gm.) every four hours; eighteen cases in group 2 received 10 grains (0.6 Gm.) every four hours for a total daily dose of 60 grains (4 Gm.). The initial dose was given at 10 a. m. on the first day. Specimens of blood and milk were collected daily immediately preceding the 10 a. m. nursing period. Quantitative determinations of free sulfanilamide were made according to the method of Marshall⁵ in the Chemical Laboratories under the supervision of F. W. Hartman. Although the method as outlined by Marshall was applicable to the analysis of the blood, a minor addition to the technic was necessary in order to obtain a clear solution for colorimetric study of the milk. Following the diazotization and coupling with dimethyl- α -naphthylamine, the milk solutions were turbid. If clear solutions were not obtained by being passed once through a high grade filter paper, refiltering through the same filter paper cleared the solution satisfactorily for comparison with the standard.

Urine and blood studies of the baby were made while nursing from mothers receiving 60 grains daily. In six babies, twenty-four hour urine specimens were collected from the fourth to the sixth day. The blood of eight babies was collected on the seventh day.

All mothers were closely observed for evidence of toxicity. Subjective symptoms were carefully noted. Objectively, attention was directed toward evidences of acidosis, optic neuritis, toxic dermatoses and gastrointestinal disturbances. When cyanosis was conspicuous, sulfhemoglobin and methemoglobin studies were made. Routine temperature and pulse and respiration rates were recorded and frequent complete blood counts were performed.

Sulfanilamide is excreted principally in the urine. With impaired renal function, urinary excretion is diminished and continued administration of the drug results in its accumulation in the body. In every case in this series the urine was normal during the antepartum and postpartum states.

Relative to the baby, particular consideration was given to (1) weight gain, (2) intake of breast milk, (3) general appearance and behavior, including persistent cyanosis, skin rashes, unusual lassitude or irritability, vomiting and diarrhea.

RESULTS

The patients in group 1 receiving 30 grains a day showed concentrations of free sulfanilamide in the breast milk which corresponded closely to the estimations in the blood stream. The level in the blood and milk ranged between 2 and 4 mg. per hundred cubic centimeters. Mothers who secreted an average of 400 cc. of breast milk daily thereby excreted approximately 8 to 16 mg. of sulfanilamide in twenty-four hours. As the blood level rose or fell in an individual case, the concentration obtained in milk tended to change propor-

tionally. The results in a case typical of this group are recorded in chart 1, in which the milk and blood values were almost identical. In only one case of our entire series was the level in the blood conspicuously higher than in the milk (table 1).

In group 2 the concentrations of the blood showed a greater daily variation, averaging from 4 to 7 mg. per hundred cubic centimeters. The values of free sulfanilamide in the milk closely paralleled those of the blood. The estimated average total daily excretion of the drug ranged from 16 to 28 mg. In contrast to the first group, concentration in the milk was generally equal to or slightly higher than the blood. Although tending to show an individual variation in milligrams per hundred cubic centimeters of sulfanilamide in the blood and milk, most results were similar to the case illustrated in chart 2.

It was with interest that we observed the results during the interval preceding engorgement of the breast. In only one case of the entire series was a high concentration of the drug present in the breast milk during

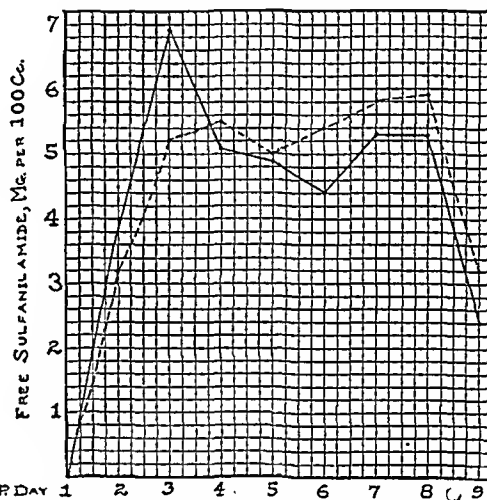


Chart 2.—Blood indicated by solid line, milk by broken line. In contrast to the first group (chart 1), concentration of sulfanilamide in the milk was generally equal to or slightly higher than the blood. Drug discontinued on the eighth day.

this period. A value of 7.8 mg. was found in the milk and 3.2 mg. in the blood. The following day the milk contained 4.1 mg. and the blood 4.4 mg., and on subsequent days the concentrations were closely parallel.

Marshall and his associates have shown that sulfanilamide rapidly disappears from the blood stream when the drug is discontinued. This study confirms theirs and also shows that the milk concentrations fall rapidly when oral administration is discontinued.

Administration of 60 grains of sulfanilamide daily to mothers produced only traces of the drug in the blood of nursing babies. Quantities ranging from 1 to 2.6 mg. per hundred cubic centimeters were excreted in the urine over a twenty-four hour period.

All babies of the entire series showed (1) satisfactory weight gain, (2) average intake of breast milk and (3) normal appearance and behavior when compared with the other babies in the nursery. From these clinical observations and the mentioned laboratory studies, it is believed that the doses and duration of administration of sulfanilamide in this study to nursing mothers were not sufficient to cause toxic manifestations in the baby.

4. Marshall, E. K., Jr.; Emerson, Kendall, Jr., and Cutting, W. C.: Para-Aminobenzenesulfonamide, *J. A. M. A.* 108: 953 (March 20) 1937.
5. Marshall, E. K., Jr.: Determination of Sulfanilamide in Blood and Urine, *Proc. Soc. Exper. Biol. & Med.* 36: 422 (April) 1937.

Varying degrees of cyanosis without sulfhemoglobin and methemoglobin was the most frequent toxic manifestation in the mothers. Mild toxic effects including general malaise, headache, occasional nausea, vertigo and tinnitus were noted in several cases. Slight elevations of temperature in five cases might have been attributed to the drug. No case of acute hemolytic anemia or agranulocytosis was encountered. Evidences

TABLE 1.—Excretion of Sulfanilamide in Blood and Milk

Case E. W.: 30 grains daily Postpartum Day	Free Sulfanilamide Mg. per 100 Cc.	
	Blood	Milk
2.....	2.1	1.2
3.....	2.6	1.5
4.....	2.5	1.1
5.....	2.7	1.6
6.....	2.3	1.8
7.....	1.8	2.0
8.....	4.1	1.0
9.....	2.8	1.6

of apparent acidosis, optic neuritis, toxic dermatoses, jaundice or other gastrointestinal disturbances were lacking.

COMMENT

In 1907 Bucura⁶ wrote that very few drugs have been demonstrated in human breast milk. Since then, thorough studies on excretion of drugs in breast milk have been occasionally reported. Most work has been directed toward qualitative determinations for a drug after oral administration. The observations of the effect on the breast-fed baby have been based on objective clinical phenomena. Recently Kwit and Hatcher,⁷ Tyson and his co-workers⁸ and others have published interesting and valuable studies on the excretion of drugs in breast milk. These workers made chemical analyses of the mother's milk but did not analyze the blood and urine of the baby. Their opinions concerning the effect on the baby were based on clinical observations. The recent publication by Hepburn, Paxson and Rogers² included quantitative determinations for sulfanilamide in the milk of the mothers and the urine of the babies. Neither concentration of the drug in the blood of the baby nor the clinical effects of sulfanilamide on the baby were stated. Adair, Hesseltine and Hac³ reported a quantitative study of sulfanilamide in breast milk. They also experimented with rabbits. In their summary they state: "Until more is known of the tolerance of the human fetus and of the newborn for sulfanilamide, the drug should be administered only with the utmost caution during pregnancy and during the period of lactation. If administered to the mother, breast feeding should be discontinued during the period that sulfanilamide is excreted in the milk"

Long and Bliss,⁹ Jones¹⁰ and Flexner¹¹ state that it is difficult to determine the dose for babies, but they estimate that a total of 1 Gm. of sulfanilamide to 10

pounds of body weight should be received during the first twenty-four hours. If one wishes to administer this amount to the baby by way of the mother's milk, enormous doses will be required. For the average baby taking 400 cc. of breast milk in twenty-four hours, a theoretical concentration of 250 mg. per hundred cubic centimeters of breast milk would give the desired 1,000 mg. daily dose. In this study, the highest dose received by a full time nursing infant on breast milk containing 7 mg. of sulfanilamide per hundred cubic centimeters was 28 mg., or approximately one-half grain (0.03 Gm.), in twenty-four hours. The amount of the drug received by the baby is so small, therefore, that therapy by way of the breast milk is not logical.

Sulfanilamide has not been pointed out as a drug of special value in the treatment of impetigo contagiosa. In four babies not included in this series impetigo developed. Sulfanilamide was administered to the mothers, and the babies received breast milk containing from 5 to 7 mg. per hundred cubic centimeters of the drug for a period of several days. No appreciable change in the course of the infection was noted.

CORD BLOOD AND AMNIOTIC FLUID

Six women received 5 grains of sulfanilamide every four hours throughout labor. At the time of delivery, specimens were obtained from the maternal blood, from the cord blood and, in three instances, from the amniotic fluid. The cord blood and amniotic fluid contained sulfanilamide in amounts closely paralleling the maternal blood concentrations, as shown in table 2.

CONCLUSIONS

1. Free sulfanilamide is excreted in human breast milk in concentrations closely corresponding to the values present in the blood stream.
2. When oral administration of sulfanilamide is discontinued, the concentration in the milk rapidly falls.
3. Breast-fed babies of full time nursing mothers did not show clinical evidences of toxic manifestations when

TABLE 2.—Sulfanilamide Concentrations in Maternal Blood, Umbilical Cord and Amniotic Fluid

Case	Free Sulfanilamide, Mg. per 100 Cc.		
	Blood	Cord	Fluid
E. H.....	5.2	5.0	...
L. B.....	3.2	3.0	...
T. R.....	2.8	2.4	...
G. B.....	1.5	1.3	1.3
A. P.....	4.7	2.7	3.3
G. R.....	0.9	0.5	1.0

sulfanilamide was present in breast milk in concentrations of 7 mg. per hundred cubic centimeters. Traces of the drug were present in the blood of the baby. The urine of these babies contained amounts varying from 1 to 2.6 mg. per hundred cubic centimeters during a twenty-four hour period.

4. A nursing baby cannot obtain an adequate therapeutic dose through the milk of a mother receiving an average clinical dose.

5. Sulfanilamide was present in the cord blood and amniotic fluid of six women following the oral administration of 5 grains of the drug every four hours throughout labor.

6. Bucura, C. J.: *Ztschr. f. exper. Path. u. Therap.* 4: 398, 1907.
7. Kwit, N. T., and Hatcher, R. A.: *Excretion of Drugs in Milk*, *Am. J. Dis. Child.* 49: 900 (April) 1935.
8. Tyson, R. M.; Shrader, E. A., and Perlman, H. H.: *Drugs Transmitted Through Breast Milk: I. Laxatives*, *J. Pediat.* 11: 824 (Dec.) 1937; II. *Barbiturates*, *ibid.* 13: 86 (July) 1938; III. *Bromides*, *ibid.* 13: 91 (July) 1938.
9. Long P. H., and Bliss, Eleanor A.: *The Clinical Use of Sulfanilamide and Its Derivatives in the Treatment of Infectious Diseases*, *Ann. Int. Med.* 11: 575 (Oct.) 1937.
10. Jones, C. C.: *A Résumé of Sulfanilamide*, *J. Iowa M. Soc.* 28: 144 (April) 1938.
11. Flexner, Morris: *Sulfanilamide: A Survey*, *Kentucky M. J.* 35: 597 (Dec.) 1937.

Clinical Notes, Suggestions and New Instruments

RESPONSIBILITY AND NEW METHOD FOR RECORD- ING DETAILED LABOR DATA

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Safe and effective amnesia and analgesia in labor must be based on individualization of each parturient patient, which in turn must depend on accurate, frequent and complete observations permanently recorded. Otherwise the patient will either be deprived of relief or, with the fetus, will be subjected to unwarranted and possibly dangerous or even fatal depression. With almost universal adoption of sedation of some sort in hospital practice, the obstetrician assumes greatly increased responsibility even in the simplest confinements and should obligate himself to show evidence of adequate personal attention to the progress of labor, not only to justify his policy of conservatism or interference, as the case may be, but also to establish a foundation for the choice of hypnotic as well as for the time, amount and method of administration, particularly in complicated labors.

In spite of these obvious truths, most labor records, even in large maternities, favor incomplete and haphazard notations divided between entries on the history by an overworked house physician and irregular recordings by a nurse who may or may not be interested or experienced in obstetrics. Ample proof of the inadequacy of such methods may be observed in the reports of maternal and fetal deaths (many of which are due to the analgesic or anesthetic used) in any mortality committee meet-

[illegible]

Record for insuring regular labor observations. Later additions include temperature, ingestions and evacuation, thereby obviating separate nurses' records.

ing, where it is often a matter of much difficulty for the patient's own physician to present a clear picture of the situation and an absolute impossibility for a stranger to unravel and evaluate the various responsible factors.

Impressed with these matters, I offer a system for recording labor observations which from thorough trial in several hospitals has proved a protection to patient, physician and nurse. The method is based on a new type of record first introduced in the obstetric department of the hospital of the University of Pennsylvania during the fall of 1935 for the purpose of continuing observations on barbituric acid amnesia (begun in 1928)¹ in labor. Through the courtesy of Eli Lilly & Co. a full time graduate nurse was employed as an obstetric attendant to note the differences in reaction chiefly with sodium pentobarbital, paraldehyde with butyl alcohol, and sodium propyl-methyl-carbonyl-allyl barbiturate-Lilly (seconal), according to the specially prepared form illustrated.

1. Drabkin, D. L.; Ravdin, I. S.; Hirst, J. C., and Lapham, M. E.: The Effect of Amytal Anesthesia upon the Uterus and Its Use in Obstetrics, *Am. J. M. Sc.* **178**: 379 (Sept.) 1929.

This system proved so satisfactory that it was utilized for further study in the Methodist Hospital and in the Preston Retreat. In the last named maternity it has remained in regular use, recently as an integral part of a folder-type history form instead of as a separate sheet. Later, on recommendation to the staff of the Philadelphia Lying-in Hospital, it was adopted there for trial in modified form and approved again recently with further modifications, having been used with a constant labor attendant in every instance of analgesia in many thousand labors. From this experience it may be stated that the system is simple and workable, with no disadvantages; I would say that it has been the means of saving a good many patients from overdosage, of allowing safe repetition of sedation in resistant persons and of providing a connected sequence of events in prolonged parturition otherwise impossible.

CONCLUSIONS

1. The use of labor amnesics and analgesics carries responsibility that can be met only by accurate, frequent and complete permanent recordings by a constant obstetric attendant and physician.
2. A specialized form here illustrated is recommended for this purpose.

500 North Twentieth Street.

THROMBOPENIC PURPURA FOLLOWING ALLYL-
ISOPROPYL-ACETYL-CARBAMIDE (SEDORMID)

DAVID B. HILL, M.D., NEW YORK

This report is submitted to record the occurrence of the manifestation of purpura in two patients who had been using sedormid (allyl-isopropyl-acetyl-carbamide) as a hypnotic.

CASE 1.—A woman aged 70 complained of the presence of peculiar looking spots in her mouth and on her skin on the morning of Nov. 21, 1936. She presented numerous purplish areas due to extravasation of blood beneath the mucous membrane, inside the lips and cheeks and on the soft palate and edge of the tongue. Several of the lesions were 1 cm. in diameter and some were oozing blood at the edges. Many petechiae were present in the skin of the extremities and body, and ecchymoses at the right elbow and forearm, with smaller areas on the other extremities. The pains experienced in both shoulders during this attack suggested probable extravasation into the joints. Physical examination was otherwise negative. The temperature and pulse rate were normal.

Examination of blood taken that morning was as follows: hemoglobin (Dare) 85 per cent or 13.6 Gm., red cells per cubic millimeter 4,530,000, color index 0.93, platelets per cubic millimeter 180,000, white cells 9,800; polymorphonuclear neutrophils 81.6 per cent (mature 78.4 per cent, immature 3.2 per cent), lymphocytes 14.4 per cent, large mononuclear cells 3.2 per cent, eosinophils 0.8 per cent and basophils 0.0. Coagulation time (Lee and White) was nine minutes and bleeding time three and one-half minutes.

During the succeeding forty-eight hours a few new lesions appeared in the mouth and on the skin, after which recovery was uninterrupted until complete about ten days later.

In June 1936, sedormid had been prescribed for insomnia and one tablet had been taken every night for a brief period. During the summer the patient was in the country and had no need of a sedative. About one week before this attack she had resumed the use of one sedormid tablet at night to promote sleep.

The cause of the patient's manifestation was at once suspected and treatment consisted of rest and the omission of any further use of sedormid. There has been no recurrence, and the patient is enjoying good health at the present time.

CASE 2.—A woman aged 48 was referred to me by a nose and throat specialist Feb. 5, 1937, because for several days she had been having epistaxis, in the treatment of which he had been unsuccessful. He expressed the belief that the major cause must be constitutional rather than local.

Having had the recent experience with case 1, I at once told him to ask her if she had been taking sedormid, and her answer

was in the affirmative. She had been upset, early in January 1937 by the death of a relative, and a friend had suggested that she use sedormid to promote sleep. For several weeks she had taken one tablet at night.

On examination, the patient showed epistaxis from a slow oozing over the entire nasal mucous membrane. Petechiae were present on the lips, soft palate, tongue and skin. There were several areas of ecchymoses on the extremities. Sedormid was at once discontinued. No new lesions developed. Epistaxis had ceased after twenty-four hours and recovery was prompt. There has been no recurrence.

115 East Sixty-Seventh Street.

A MODIFICATION OF THE ASCHHEIM-ZONDEK TEST

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GREAT FALLS, MONT.

The Aschheim-Zondek test for the diagnosis of pregnancy is one of the most satisfactory, useful and accurate laboratory tests that have been developed within a generation.

Rats have largely replaced mice, used in the original test, since only one rat is used for the test rather than five mice.

The Friedman test has the advantage over the Aschheim-Zondek test in that the results are known in from twenty-four to thirty hours rather than on the fifth day, as in the original Aschheim-Zondek test. However, when large numbers of tests are performed the inconvenience of keeping on hand large numbers of isolated rabbits is a matter of no small concern.

We have found that, if young female white rats are used, the test may be completed in thirty hours, the advantage in time of the Friedman test thus being gained without the inconvenience of keeping isolated rabbits on hand.

We have used young female white rats from 30 to 45 days old. Instead of injecting 0.5 cc. of urine subcutaneously twice a day on three successive days and killing the animal on the fifth day, we have injected 1.5 cc. of urine subcutaneously (in the groin) three times in a single day and killed the rat thirty hours after the first injection. As a control, we have in each instance carried out the test on another rat which received two subcutaneous injections of 1.5 cc. of urine daily for three days and was killed on the fifth day.

In 153 tests in which both methods were used, the results were identical. In no case in which a positive result was secured by giving two subcutaneous injections of 1.5 cc. of urine daily for three days and killing the animal on the fifth day was the test other than positive in the rat that had received only three injections of 1.5 cc. of urine and been killed thirty hours after the first injection.

We believe that this slight modification of technic "speeds up" the Aschheim-Zondek test without affecting its accuracy and makes it more practical than the Friedman test.

The detailed technic of our modification of the Aschheim-Zondek test follows:

1. The morning specimen of urine is collected.
2. A female white rat from 30 to 45 days old is injected with 1.5 cc. of urine three times during the day.
3. Thirty hours after the first injection the animal is killed with chloroform and the ovaries are examined.
4. In positive cases the ovaries are enlarged and hyperemic and show hemorrhagic follicles.

Medical Arts Building.

The Indispensable Amino Acids.—The following amino acids have been classified as indispensable with respect to their growth effects: lysine, tryptophan, histidine, phenylalanine, leucine, isoleucine, threonine, methionine, valine and arginine. The following amino acids are classified as dispensable: glycine, alanine, serine, norleucine, aspartic acid, glutamic acid, hydroxyglutamic acid, proline, hydroxyproline, citrulline, tyrosine and cystine.—Rose, William C.: *The Physiology of Amino Acid Metabolism*, *Proc. Inst. Med. Chicago* 12:98 (April 15) 1938.

Special Clinical Article

ANTEPARTUM CARE

CLINICAL LECTURE AT SAN FRANCISCO
SESSION

OTTO H. SCHWARZ, M.D.

ST. LOUIS

Although the United States was one of the first countries to develop antepartum care, much yet remains to be done to have such care reach the great majority of the mothers in our land. No better introduction can be given a discussion of antepartum care than to recall the classic statement of Williams concerning this subject, that from a biologic point of view pregnancy and labor represent the highest function of the female reproductive organs and should be regarded as a normal process. However, when one recognizes the marked changes in metabolism during pregnancy and the numerous changes that take place in the expectant mother, the borderline between health and disease is not so distinct as at other times. Derangement so slight as to be of little consequence in ordinary circumstances may readily be the precursor of pathologic conditions which may seriously threaten the life of the mother and her child. Antepartum care, therefore, may be defined as the care and supervision of the pregnant woman; the broader term maternal care would be better to include both labor and the puerperium.

I shall not go into great detail concerning this care—these details are enumerated in every standard textbook—but shall emphasize only the more important points that this care involves. It is obvious that the patient must report as early as possible in pregnancy. A thorough general physical examination should be carried out early in pregnancy in order to recognize or eliminate medical complications. The medical complications that give most concern are heart disease, tuberculosis, diabetes and hyperthyroidism. They are in themselves problems, but superimposed on pregnancy they represent a serious picture and each case becomes an individual problem which must be carefully managed.

Fortunately today, with improved medical care, the pregnant woman can go through this ordeal in most instances with little or no increased danger as regards her life expectancy, and only occasionally does the question of termination of pregnancy arise. In a clinical practice these patients are best seen on special days by both the obstetrician and the internist. In order to have a better understanding of the existing condition and its prognosis, it is best to hospitalize the patient when first seen, the length of stay in the hospital depending on the severity of the condition. Cardiac and nephritic patients are brought in several times during their pregnancy, and it is ideal to have them in the hospital at least two weeks before delivery. Active tuberculosis in pregnancy should be handled as active tuberculosis is handled under any other condition. If the proper treatment is instituted early, these patients during pregnancy do as well as and sometimes better than in the nonpregnant state. However, it must be borne in mind that unrecognized active tuberculosis in pregnancy will

Read in the General Scientific Meetings at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 13, 1938.
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progress rapidly in the untreated state. Therefore it is important to recognize early active lesions.

Diabetes today, so far as the mother is concerned, can be well managed, but in spite of the use of insulin the fetal mortality had not been improved until very recently. Labor is quite an ordeal for the fetus of the diabetic mother and, owing to marked derangements in carbohydrate metabolism, hypoglycemia frequently develops in the fetus after birth and, unless it is counteracted, may result in death. Babies of diabetic mothers are large as a group and contain more fat than those of normal mothers. Difficult labor, therefore, is frequently encountered. On this account it has been suggested in various quarters that pregnancy be terminated by cesarean section, under local anesthesia, at about thirty-eight weeks. Figures show a marked lowering of fetal mortality in cases handled in this way.

Repeated pregnancies with medical complications should definitely be avoided. Although the mother may go through one pregnancy with little additional risk, this does not usually hold for repeated pregnancies, so that in any event future conception is highly undesirable, not only from the point of view of the mother's health but for economic and social reasons as well.

It is important to recognize pelvic abnormalities early in pregnancy; not only the contracted pelvis but the presence of pelvic tumors should be determined because, if intervention is indicated, they can best be handled early in pregnancy. In the first trimester of pregnancy it is important to have information concerning the position of the uterus. If it is retroverted, it should be brought forward and held there with a properly fitting pessary until the patient is a little over twelve weeks along. If the patient is not seen in the first few weeks of pregnancy, the retroverted uterus will frequently adjust itself; but occasionally it may become incarcerated, giving rise to serious signs and symptoms, owing to the cervix rising up behind the symphysis. Under such circumstances the urethra is markedly lengthened and pressure is exerted at the base of the bladder. This leads at first to frequency of urination and then to retention of urine. In extreme cases there may be complete anuria with a greatly distended bladder. On account of the markedly lengthened urethra, the bladder can be emptied only by means of a male catheter.

The classification of the pelvis should be determined by routine examination. Although marked rachitic deformities are seen only occasionally today, certain types of moderately contracted pelves, namely the generally contracted and simple flat, give rise to dystocia. Arrangements should be made for the hospitalization of patients presenting such conditions so that they may have the proper test of labor under the best conditions. It may be said here that antepartum care and supervision are of no great value unless preparations are made for a safe and intelligent conduct of labor.

To emphasize this point, one need only refer to the statistics on maternal mortality, and most striking of all these is the Rothert report of some five years ago. This report consisted of a study of the causes of death for a two year period in fifteen states. In this area there were 7,380 deaths due to puerperal causes, of which 2,948, or 40 per cent of the deaths, were due to infection and 1,900, or 26 per cent, were due to the late toxemias of pregnancy. Antepartum and postpartum hemorrhage were third, but fortunately comprised only 6.7 per cent of the total maternal mortality.

It is obvious that, with good antepartum observation and proper care at the time of delivery, many of these infections could be reduced, but it is incorrect to state that they could be reduced to a negligible minimum for the simple reason that many infections which occur during difficult and traumatizing labor occur from organisms that the patient harbors herself.

On the other hand, the prevention of serious cases of toxemia of pregnancy can be readily accomplished by the proper antepartum care, as is shown by the low incidence of these conditions in any well conducted private practice. It is interesting to point out that in the 7,380 cases there was information obtainable on 5,636 cases as regards antepartum care. According to this report, antepartum care is divided into three grades: grade 1 is accepted as adequate antepartum care, grade 2 indifferent antepartum care, and grade 3 poor antepartum care. In this group of 5,636, only 725 were given grade 1 care, 499 were given grade 2, and 1,337 were given grade 3, and there was no antepartum care in 3,025.

It is also interesting to mention conditions under which patients dying of the toxemias of pregnancy were first seen. In the whole group, 35 per cent were first seen in coma or convulsions. Patients coming in poor condition brought the total up to 60 per cent, and only 20 per cent were in good condition when first seen. The white patients in the city showed the best record, but in this group 20 per cent were seen in coma and convulsions and up to 45 per cent in poor condition. White patients in rural districts were somewhat worse off, 30 per cent being admitted in coma and convulsions and up to 60 per cent in poor condition. This is interesting, because in most large cities adequate facilities for proper antepartum care are available, and it means only that patients who had such service available did not take advantage of it. Of the Negro patients in this group in the rural districts 60 per cent were admitted in coma and convulsions and in the city 45 per cent. Of the Negro patients in this group in poor condition 90 per cent were admitted from rural districts and 80 per cent from the city.

What can be accomplished by good antepartum care is outstandingly shown in the symposium on the prevention of eclampsia which was given at a recent meeting of the American Gynecological Society, but before taking this up I wish to make a few remarks concerning the treatment of eclampsia once this condition is present in a fulminating state. Although there has been marked improvement in the treatment in most cases, the mortality rate is still high. Twenty years ago in most clinics it was between 20 and 30 per cent, but today it is in the neighborhood of 10 per cent. Some few, such as McCord of Atlanta, present figures as low as 6 per cent for a large series of cases.

The cause of eclampsia is not known, but the treatment is far from empirical because the treatment aims at abolishing certain existing signs and symptoms. Obstetricians have relied chiefly on elimination and the use of intravenous dextrose and magnesium sulfate, resorting to cesarean section under local anesthesia only if the patient does not improve on the conservative regimen. I do a cesarean section in about one in every six cases. That no ideal method of treatment has yet been found is shown clearly in that at every clinic in this country the treatment varies to some degree, but magnesium sulfate and dextrose seem to be the most freely used procedure.

In normal pregnancy there are many physiologic changes. In many instances these become greatly exaggerated in the late toxemias and especially in eclampsia. Of these, marked retention of sodium chloride and edema are very striking. It has long been known that in limiting the intake of salt during the last half of pregnancy the physiologic rise in weight can be checked. In eclampsia, edema and retention of salt are most marked, and although the hepatic lesion, which is a specific one in eclampsia, is found in most cases at autopsy, this condition is probably terminal and has little or nothing to do with the onset of the disease, the retention of salt and edema being in all probability more concerned with the oncoming convulsions.

What can be prevented by good antepartum care is very definitely shown in the figures of de Snoo of Utrecht, Holland, which were presented at the meeting of the American Gynecological Society in 1937. Over a ten year period in his clinic there were 20,000 deliveries with twenty-seven puerperal deaths and not a single death due to eclampsia. This is an unusually good record and, of course, may not be repeated in the next 20,000 births. In these 20,000 clinical births, eclampsia developed in twenty-one mothers and in almost every instance it was due to lack of cooperation on the part of the patient. This remarkable record was obtained chiefly by putting the patients on absolutely salt-free diets as soon as signs of toxemia developed. For some time I have been restricting salt in such cases, but not quite to the degree emphasized by de Snoo. I have emphasized also the abstinence from meat protein and good elimination through the bowels. During a period of six years in which there were approximately 12,000 deliveries, 217 cases of preeclampsia developed. Of these 217 cases, eclampsia developed in twenty-six, with two deaths. The patient's lack of cooperation precipitated the onset in most instances.

With the remarkable record of de Snoo in mind, it behooves the profession to emphasize further the value of antepartum care, so far especially as the late toxemias of pregnancy are concerned. In St. Louis there are at least ten well established clinics, and in spite of the fact that these are available to the public they are not used to full advantage by the patients. A discussion by Daily in the aforementioned symposium indicates how improvement can yet be made so far as toxemias are concerned. He states that in the years 1930-1935, 36.8 per cent of the maternal deaths were due to the late toxemias of pregnancy, and in a comparison of 1930 with 1935 there was a marked decrease in the number of maternal deaths, eclampsia accounting for 54 per cent of this decrease. In 1935 in urban areas it was reduced to 15.4 per cent, while in the rural districts it was 23.6 per cent of all puerperal deaths.

In a report by Dr. Franz Arzt of the analysis of deaths from puerperal causes for three years in St. Louis, twenty-eight maternal deaths, or 13.5 per cent, were due to eclampsia. During this time there were approximately 40,000 births. In the cases handled exclusively by the municipal antepartum clinics for the three years, numbering 4,479, there were no deaths due to eclampsia among the white patients and three among the Negroes. Although this record for the city as a whole is comparatively good, further improvement should be expected. To bring about this improvement further education of the public is necessary. The patients must be instructed to come early and cooperate fully with the outline of care that is prescribed.

Perhaps one of the reasons that cooperation is not as good as it should be is that the procedures which actually prevent the development of fulminating eclampsia are so commonplace, namely the restriction of meat, catharsis and limiting of salt. If the patient could be made to see how very much these rather commonplace procedures will do to ward off serious cases of toxemia, the death rate due to the development of eclampsia, with its definite mortality, might be reduced to an almost negligible minimum.

630 South Kingshighway Boulevard.

Special Articles

THE CHEMISTRY OF VITAMIN C

C. G. KING, Ph.D.

PITTSBURGH

This article and others recently published or to be published comprise a new series on the present status of our knowledge of the vitamins. They have been prepared under the general auspices of the Council on Pharmacy and Chemistry and the Council on Foods. The opinions expressed are those of the authors and not necessarily the opinions of either council. Reprints are not available but the articles will be published later in book form.—Ed.

IDENTIFICATION

A primary requisite for studying the chemical nature of vitamin C was provided by Holst and Frölich¹ when they observed that the guinea pig could be used as an experimental animal for the study of scurvy. The experimental diets and general technic developed by Cohen and Mendel² and La Mer, Campbell and Sherman³ then made it possible to measure antiscorbutic activity in a satisfactory quantitative manner, free from interference by deficiencies in other essential nutrients. Attempts to isolate the vitamin from natural products encountered great difficulty, however, because of its extreme sensitiveness to destruction by oxidation.

By 1931 many investigators, particularly Zilva and his associates,⁴ Bezssonoff and his associates⁵ and King and his associates⁶ had succeeded in concentrating the vitamin to such a degree that approximately 1 to 2 mg. of solids daily served to protect young guinea pigs from scurvy. The isolation of the vitamin from lemons and its identification as "hexuronic acid," having a protective level of 0.5 mg. a day, by Waugh and King⁷ in 1932 was followed within a few weeks by a report from Svirbely and Szent-Gyorgyi⁸ that 1 mg. daily of

- From the Department of Chemistry, University of Pittsburgh.
1. Holst, A., and Frölich, T.: *Experimental Studies Relating to Ship Beriberi and Scurvy*, J. Hyg. 7: 634, 1907.
 2. Cohen, B., and Mendel, L. B.: *Experimental Scurvy of the Guinea Pig in Relation to the Diet*, J. Biol. Chem. 35: 425 (July) 1918.
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 6. Smith, F. L., and King, C. G.: *The Preparation and Storage of Vitamin C Concentrates from Lemon Juice*, J. Biol. Chem. 94: 491 (Dec.) 1931. Svirbely, J. L., and King, C. G.: *The Preparation of Vitamin C Concentrates from Lemon Juice*, *ibid.* 94: 483 (Dec.) 1931.
 7. Waugh, W. A., and King, C. G.: *The Chemical Nature of Vitamin C*, Science 75: 357 (April 1) 1932; *The Isolation and Identification of Vitamin C*, J. Biol. Chem. 97: 325 (July) 1932; *Proc. Am. Soc. Biol. Chem.*, April 1932.
 8. Svirbely, J. L., and Szent-Gyorgyi, Albert: *Hexuronic Acid as the Antiscorbutic Factor*, Nature 129: 576 (April 14) 1932; *Biochem. J.* 26: 865 (No. 3) 1932.

"hexuronic acid" prepared from adrenal glands was protective against scurvy. The protective value of hexuronic acid prepared from adrenal glands by Kendall,⁹ using an entirely different procedure, was then shown by Waugh and King¹⁰ to be identical with that of the product from lemons, thereby essentially removing any question of contamination of the original crystals by another active substance. In their next paper Svirbely and Szent-Gyorgyi¹¹ also found the minimum protective level of their product to be 0.5 mg. a day. Within a short time the identity of the vitamin was independently confirmed by several laboratories, particularly those of Tillmans,¹² Vedder,¹³ Nelson,¹⁴ Harris¹⁵ and von Vargha.¹⁶ The compound $C_6H_8O_6$, having the same general formula and many properties in common with other hexuronic acid lactones, had been prepared from cabbage, oranges and adrenal glands in 1928 by Szent-Gyorgyi¹⁷ in studying tissue respiration systems, but there was no knowledge of its antiscorbutic value previous to the work published in 1932.

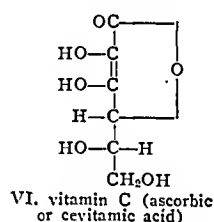
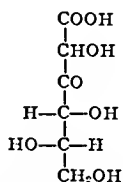
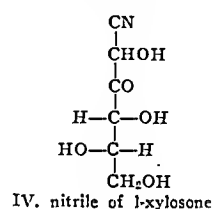
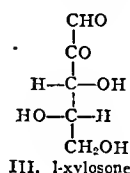
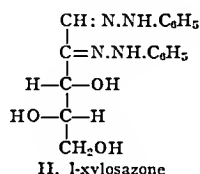
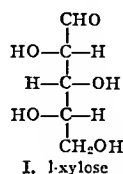
It may be interesting to note that isolation of vitamin C resulted, in one laboratory, from four years of systematic fractionation of lemon juice, based entirely on biologic assays, and that in another laboratory biologic assay for vitamin function was reported five years subsequent to the isolation of the vitamin as hexuronic acid, a silver nitrate-reducing agent in tissues, and two years after its negative assay as a hormone.

STRUCTURE AND SYNTHESIS

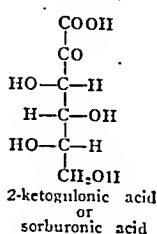
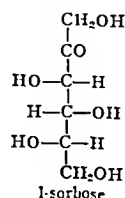
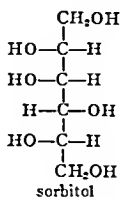
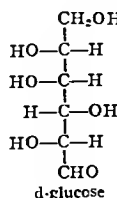
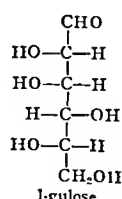
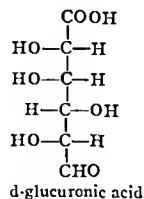
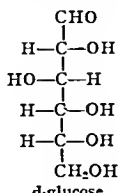
The structural formula of the vitamin was established in 1933, primarily by Haworth, Hirst and his associates,¹⁸ Karrer and his associates,¹⁹ Micheel and Kraft²⁰ and von Euler and Klusmann,²¹ using material obtained from adrenal glands and paprika, supplied largely from Szent-Gyorgyi's laboratory. Before the structure was established with certainty, Reichstein, Grussner and Oppenauer²² succeeded in synthesizing the *d*- and later the *l*- form of the acid. Some delay and confusion occurred in working out a satisfactory graphic formula, because the vitamin represented an entirely new type of configuration for a hexuronic acid lactone. Before the structural formula had been established, so that the acid could be named according to its relationship to known sugars, Haworth and Szent-

Gyorgyi suggested the name "ascorbic acid"²³ to connote its antiscorbutic nature. The American Medical Association introduced the name "cevitamic acid" expressly to avoid this connotation.

Synthesis was first accomplished from *l*-xylose, I. On treatment with phenyl hydrazine *l*-xylose yields the osazone, II. This compound on hydrolysis yields *l*-xylosone, III. Treatment of the latter with hydrocyanic acid produces the nitrile of the *l*-xylosone, IV, which on hydrolysis is converted first into the intermediate 2-ketogulonic acid, V. In an acid medium lactonization and enolization occur and vitamin C itself, VI, is produced.



Several different methods of synthesis have been published in detail and others have been disclosed only in patents. The catalytic and electrolytic reduction of *d*-glucose to sorbitol on a commercial scale, followed by selective fermentation to *l*-sorboside, provides a basis for commercial synthesis at low cost. A number of procedures have been followed for converting sorbose to the intermediate sorburonic or 2-ketogulonic acid. The more important structurally related compounds are *d*-glucose, *d*-glucuronic acid, *l*-gulose, sorbitol, *l*-sorboside and sorburonic acid.



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10. Waugh, W. A., and King, C. G.: The Vitamin C Activity of Hexuronic Acid from Suprarenal Glands, *Science* 76: 630 (Dec. 30) 1932.

11. Svirbely, J. L., and Szent-Gyorgyi, Albert: The Chemical Nature of Vitamin C, *Biochem. J.* 27: 279 (Feb.) 1933.

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Comparison of the formulas for *d*-glucose, *l*-gulose and *l*-sorbose serves to illustrate the transition in series from *d*- to *l*- in going through the *d*-glucose \rightarrow sorbitol \rightarrow sorbose steps, since the *d*- or *l*- nomenclature is based on the configuration of the asymmetric carbon farthest from the saccharide group. Antiscorbutic activity is contingent on the *d*- configuration of C-4 (responsible for its dextrorotation) and the *l*- configuration of C-5. A number of sugar derivatives having structures analogous to that of ascorbic acid (2,3-enediol-4-lactone) have been prepared and shown to have similar chemical properties. Zilva²⁴ has given a good summary of the relative physiologic values of closely related synthetic substances, the most active being *l*-rhamnoascorbic acid, which had one fifth of the antiscorbutic value of ascorbic acid. None of the other compounds examined had more than one tenth of the value of ascorbic acid. *d*-Ascorbic acid had no antiscorbutic value.

TYPE REACTIONS

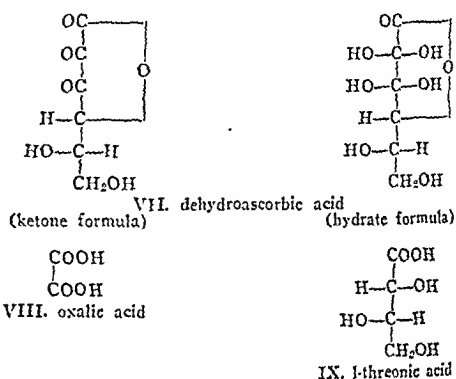
The acidic properties of the vitamin are due to dissociation of an enolic hydrogen rather than to opening of the lactone ring. Methylation with diazomethane involves the enolic groups (C-2 and C-3) first, and further treatment with dimethylsulfate forms ethers from the other two OH groups (C-5 and C-6). Esterification of the alcohol groups on C-5 and C-6 can be accomplished readily with acyl halides. The carboxyl group does not enter into any of the common laboratory reactions of the vitamin in either aqueous or alcoholic solution. The lactone ring of dehydroascorbic acid apparently opens more readily than that of ascorbic acid. Condensation with aldehydes, acetone and other ketones takes place under the influences of very mild dehydrating agents, giving rise to stable compounds that can be crystallized readily from acetone, alcohol and other organic solvents. Triphenylmethylchloride forms an ether (trityl) readily on carbon-6. Heating with strong mineral acids gives rise to furfural and carbon dioxide.

The reactions of greatest general interest are those dealing with oxidation and reduction. Barron, De Meio and Klemperer have shown that in aqueous solution below p_H 7.6 the vitamin is not oxidized on exposure to air unless the reaction is catalyzed by traces of copper²⁵ or some other activating agency. Although copper had been widely recognized as a very effective catalyst, their results were of special interest in showing that the vitamin is nonautoxidizable within the normal p_H range of plant and animal tissues. The interdependence of p_H , anions and concentration of copper in their relation to the rate of aerobic oxidation has been demonstrated by Lyman, Schultze and King.²⁶

As would be expected from its oxidation-reduction potential, the vitamin is reversibly oxidized by a great many organic compounds such as methylene blue, quinones and the indophenol dyes, and by inorganic reagents such as Cu^{++} , Fe^{+++} , Hg^{++} , Ag^+ , Mn^{+++} , $Fe(CN)_6^{--}$, NO_3^- , WO_4^{--} , H_2O_2 , and I_2 . A discussion of the use of oxidizing agents for the quantitative esti-

mation of vitamin C in tissues will be found in the section on methods of assay. The dry crystals of vitamin are stable on exposure to air and daylight at room temperature through a period of several years. They tend to become buff colored without undergoing appreciable decomposition. In aqueous solution, however, the rate of aerobic oxidation is greatly accelerated by exposure to light, especially in the presence of flavins.

Dehydroascorbic acid, VII, the reversibly oxidized product formed from ascorbic acid, is fairly stable in acidic aqueous solutions, e. g. below p_H 4, but in faintly acid (p_H above 4), neutral or alkaline solutions it undergoes an irreversible rearrangement, giving rise to another strong reducing substance. It is this second strong reducing substance, as shown particularly by the work of Borsook and his associates,²⁷ that gives rise to oxalic acid, VIII, and *l*-threonic acid, IX, on further oxidation.



Reduction of dehydroascorbic acid can be accomplished readily by H_2S , cysteine, glutathione and the "fixed-SH" groups associated with proteins. The rates of reduction are markedly dependent on the relative concentrations and the p_H of the solutions, however. Metals reacting with acids, or hydrogen under pressure with common catalysts do not reduce the product with good yields.

PHYSICOCHEMICAL PROPERTIES

When adequately protected from oxidation, the vitamin can be crystallized from solution in water or the lower alcohols, acetone, ethyl acetate and many other organic solvents. The colorless crystals tend to form dense radiating clusters but may form characteristic plates or needles (monoclinic, pseudo-orthorhombic), depending on the solvent and the rate of crystallization.

Its physical constants are: melting point 192 C.; specific rotation $+24$ degrees in water, 48 degrees in alcohol, without mutarotation; acidic dissociation $pK_1 = 4.17$ (Harris et al.) (or 4.20 cf. Ball), $pK_2 = 11.57$; absorption maximum 260 millimicrons in water, 263 millimicrons in alcohol (Karrer, Hirst, et al.); oxidation-reduction potential (Borsook) at p_H 4.0 and 35 degrees, $E_{\frac{1}{2}} = +0.166$ V. Ball gives $+0.390$ volts for the normal potential of ascorbic acid at 30 degrees, and five minutes for the half life of dehydroascorbic acid at p_H 7.24, 30 degrees. For a detailed discussion of the oxidation-reduction potentials under various conditions, the recent papers of Borsook and his associates²⁷ and of Ball²⁸ should be consulted.

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THE PHARMACOPEIA AND THE
PHYSICIAN

LOCAL URINARY ANTISEPTICS

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This is one of a series of articles written by eminent authorities for the purpose of extending information concerning the official medicines. The twenty-four articles in this series have been planned and developed through the cooperation of the U. S. Pharmacopoeial Committee of Revision and THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION.—ED.

In the application of local antiseptics to disorders of the urinary tract, a twofold purpose must be kept in view; first the destruction of the infecting microorganisms, and second the stimulation of a reaction in the tissues of the patient which will enable him to offer the necessary resistance to the infection. It is now generally recognized that the stimulation of the natural resistance of the mucous membrane of the urinary tract is quite as important as the destruction of the infective agents. If, for example, an antiseptic is wrongly used in the urethra, it may, while slaying the gonococcus, incidentally so damage the normal epithelium as to invite future stricture formation. Rightly used, it will offer the mucous membrane just enough irritation to stir it to defend itself but no more. This happy mean is what the urologist is seeking. In the past the physician's zeal to kill off the intruding organisms often got the better of his discretion and resulted all too frequently in the exhaustion of the patient's powers of resistance by the violent insults to which the delicate membrane of this sensitive tract was subjected.

Much has been learned from past mistakes. It is now known that the medication addressed to these tissues should be the mildest that is consistent with effectiveness. An active participation of the host is essential for the success of attempts at antisepsis. The urinary tract must become the uncongenial place for the habitation of these organisms. This will of necessity be a gradual process, requiring the utmost gentleness and patience. There is no way of knowing in advance the type of reaction that will result from the use of a particular medicament in a given individual. Nothing is more difficult than to estimate the value of an antiseptic in either the prevention or the treatment of a septic process. One must proceed with the greatest care in each individual case.

One of the greatest difficulties at the outset lies in the fact that the infecting organisms have usually penetrated so deeply into the tissues before treatment has been started that the local antiseptic cannot follow them. In one's choice of treatment, one has to consider not only the bacteriostatic powers of a given substance and the degree of irritation that it is likely to produce in the mucous membrane but also its capacity for penetrating the latter. Few of the older antiseptics could exert more than a superficial action on the epithelium, and too often this structure was ruthlessly destroyed without the organisms sharing in the destruction.

In this study I shall review the most important of the local urinary antiseptics in use at the present time and shall then make an attempt to evaluate their usefulness in the separate portions of the urinary tract. In

order to do this I shall take up in succession the consideration of acute and chronic urethritis, acute and chronic cystitis and acute and chronic pyelitis (pyelonephritis), in relation to the appropriate local antiseptic treatment of each.

The substances used in local antiseptic treatment of the urinary tract fall, in a general way, into groups of (1) mercurials, (2) silver salts, inorganic and organic, (3) dye therapy and (4) chemotherapy, although the members of these groups overlap at some points. In addition, and not falling precisely into any one of the groups, there are such time-honored remedies as potassium permanganate, boric acid, phenol, cresol, trinitrophenol (picric acid) and various other more or less widely used drugs.

ANTISEPTIC TREATMENT

These various substances may be used either as irrigations or as instillations or injections. The purpose of an irrigation is not only the introduction of a medicament to the tissues but also, and in large degree, the removal of debris and detritus. It is held by some urologists that the nature of the medicament introduced is relatively inconsequential, the main idea being to cleanse the tract involved. Solutions introduced as irrigations are comparatively weak, their frequent repetition rather than their strength being relied on to make them efficacious. An instillation, on the other hand, consists of a small quantity of stronger concentration of the antiseptic substance designed to be retained in an organ from five minutes to several hours, as the case may be, to exert its full medicinal properties on the tissues. The determination of the proper strength is of overwhelming importance. Some of these substances cannot be used in a strength that is bactericidal and yet one sees the infection clear up in response to them. Evidently the good results are due to some reaction within the mucous membrane.

Acridine (U. S. P.).—Neutral acridine is a popular drug now in common use. Chemically it is 2, 8 diamino-10-methylacridinium-chloride and 2, 8 diaminoacridine. When properly diluted it is not irritating, and in selected cases its use has given extremely satisfactory results. If used in too strong concentration it readily invites stricture, owing to chemical inflammation of the tissues. It is deceptive, and many patients will not tolerate it. Too long continued or too frequent use is also to be avoided. One injection a day is all that should be risked.

Mercurochrome (N. N. R.).—This dye has been decidedly popular for a good many years as a urinary antiseptic for local use. It is the disodium salt of 2:7-dibromo-4-hydroxymercurofluorescein. If administered in low dilution not more than once a day for not more than three days in succession it is not irritating. It generally requires a follow up by some accompanying milder drug, such as mild protein silver. In too large dosage, however, or if given too often, its irritative properties come to the front.

Gentian Violet Medicinal (N. N. R.).—This is one of the rosaniline dyes, with low toxicity for the tissues and excellent capacity for penetration. Its relative harmlessness has been proved by the observation that tissue cultures are not injured by concentrations that arrest bacterial growth. It is particularly successful in anterior urethral infections of a nonspecific nature.

Potassium Permanganate (U. S. P.).—This most common of all antiseptic astringents acts directly on the gonococcus. It has in addition an indirect action

by causing edema of the mucosa of the urethra, which helps to destroy the organism. In the presence of organic material potassium permanganate is rapidly reduced to inactive manganese dioxide, setting free nascent oxygen. It is during this process that the gonococcal action occurs. If much organic material of a nonbacterial nature (such as pus and blood) is present, the reduction is quickly accomplished and there is no more power to destroy cocci. Its germicidal power is, therefore, not high, but because of its admirable capacity for cleansing it continues to remain in favor. By its ability to oxidize dead matter, plugs of mucus, pus and dead epithelium are loosened up and proper drainage is established. It should be used as hot as the tissues can bear. Its action is exerted more in the anterior than in the posterior urethra.

Zinc Permanganate (N. N. R.).—This lesser used zinc salt of permanganic acid should be better known. It resembles the potassium salt in its oxidizing properties (only it gives up oxygen more easily than does the potassium salt) and is more astringent.

Boric Acid (U. S. P.).—Although in reality not germicidal, boric acid is such an admirable cleanser that no discussion of this kind would be complete without including it. From time immemorial it has been a dependable agent for lavage of cavities in which sterile water or saline solution would have been more irritating. The absence of all toxic effect makes it an ideal irrigating fluid where bulk is desirable for cleansing or distention. It is nonirritating, stable and of simple chemical structure. Though not a disinfectant, even in saturated solution, it checks putrefaction and decomposition in a solution of 0.3 per cent. In urologic practice it is used as a routine by many for cleansing of the bladder or urethra before an instillation of some antiseptic substance.

Of all the substances employed today as local urinary antiseptics, the various silver compounds enjoy the widest popularity. Starting with silver nitrate, which still remains as the keystone of the structure of local antisepsis, there is now available a long array of derivatives, each of which has its partisans and all of which produce good results when properly administered.

Silver Nitrate (U. S. P.).—The inorganic salts of silver, of which silver nitrate is the best known and most useful, form resistant precipitates with proteins, so that their local action is easily controlled. The antiseptic effect of silver nitrate is high, its toxicity low. In the presence of the tissues of the body, silver surpasses mercury, since its protein compounds, as well as the colloidal oxides and metallic silver, liberate a small amount of silver ions. The antiseptic action of silver nitrate goes quite deep, since it forms easily soluble double salts of silver albuminates and sodium chloride in the tissues. Its caustic and astringent action may be stopped with sodium chloride. It acts on the urethra by liberating nitric acid and coagulating albumin. It also exerts an indirect influence in stimulating the mucous membranes wherever it is introduced into the urinary tract. A reaction is necessary in the form of slight burning. This irritant character contraindicates its use in some cases but increases its value in others. If any chlorides are present in the urine, it is immediately precipitated in the form of inactive silver chloride. This makes its action on the urinary tract only momentary. It should therefore be reserved for cases in which an irritative or caustic effect is desired.

Out of silver nitrate came derivatives in the form of colloidal suspensions, the use of which in the urinary tract avoids the irritation, pain, astringency and corrosion associated with the inorganic salt. The activity of these preparations is said to be quite independent of their total silver content and is determined by the ion concentration, which differs for different compounds. When antisepsis without irrigation is desired, the direct application of the colloid compounds may have advantages over their indirect production from silver nitrate within the tissues. Some of these colloids retain a certain degree of irritant property, while others become entirely bland. Thus there are strong and mild silver proteins, the former retaining in part the irritant quality of silver nitrate, while the latter have lost it. The clinician has, therefore, at his disposal a wide range of colloidal silver compounds that can be employed to meet the needs of the individual case.

Strong Protein Silver (U. S. P.).—These proteinates have the lowest percentage of silver (from 7 to 8.5 per cent), but in solutions this becomes largely ionized, so that they have the strongest bacteriostatic effect but are also distinctly irritant, though far below the silver nitrate in this respect. The irritant effect of this preparation, originally introduced under the name of protargol, is about one tenth that of silver nitrate, confirming the fact that nearly all the silver is ionized. The strong silver proteins thus lie therapeutically between silver nitrate and mild protein silver. All these colloidal silver preparations consist of finely divided metallic silver in colloidal suspension with a protective colloid of some albuminoid substance to maintain the suspension. They apparently do not penetrate deeply but have a definite antiseptic value on mucous membranes. They act by producing an intense hyperemia, causing a serous exudate and active phagocytosis, which sweeps away both living and dead organisms. All these solutions should be made freshly every day or two, since they deteriorate on standing, and they should be kept in amber colored bottles.

Mild Protein Silver (U. S. P.).—With slight variations this group contains such preparations as argyrol, neosilvol and other colloidal compounds of silver oxide and a protein derivative. It differs from strong protein silver in being entirely nonirritant. It is also less active as an antiseptic but more soothing. The high specific gravity of its solutions facilitates their spreading, enabling them to act as detergents for the removal of pus and secretions. Mild protein silver contains from 19 to 25 per cent of silver. The different brands differ slightly in composition but are essentially equivalent in therapeutic properties, all being mucilaginous demulcents.

ACUTE URETHRITIS

The local antiseptic treatment of acute urethritis naturally falls into two categories, according to whether one is dealing with a gonococcal infection or an infection of nonspecific origin. These again have to be differentiated for purposes of treatment into male and female conditions and, in the male, into treatment of anterior and of posterior urethritis.

Anterior Gonococcal Urethritis.—The commonest acute urethritis is, of course, that due to gonococcal infection in the anterior urethra of the male.

With the first appearance of a urethral discharge, an attempt may be made to abort the attack, if not more than a few hours to a day has elapsed. Either one of the solutions given in prescriptions 1 and 2 may be used for injections.

After the patient has urinated, 8 cc. is slowly injected, to be retained five minutes, then evacuated, and the procedure repeated three or four times. For subsequent treatment in early stages it is used in tenth-normal strength three or four times daily. If the gonococci have not disappeared by the third day, the treatment has failed to abort the infection and further measures must be taken addressed to the acute

PRESCRIPTION 1.—Solution of Mild Protein Silver

R Mild protein silver.....	12 Gm.	5ijj
Distilled water, q. s.....ad	120 cc.	flʒiv

PRESCRIPTION 2.—Solution of Strong Protein Silver

R Strong protein silver.....	2.40 Gm.	gr. xxxiv
Distilled water, q. s.....ad	120.00 cc.	flʒiv

(These should be freshly prepared.)

inflammatory stage of urethritis. These will be largely internal. After about three days, when the most acute phase has abated, the hand injections may be resumed, in from one-tenth to one-fourth normal strength. Once a day the physician may instill a more irritative antiseptic, such as neutral acriflavine 1:5,000 or zinc permanganate 1:4,000, of which 6 cc. is to be retained one minute. Many physicians prefer an instillation of potassium permanganate 1:8,000.

Either mild protein silver 5 to 15 per cent or strong protein silver 0.25 to 1 per cent may be instilled. Generally speaking, the strong protein silver may be instilled in strengths of from 0.25 to 1 per cent in the urethra, and the mild protein silver in from 5 to 10 per cent; this should be done every two to four hours, if possible. Solutions should have been recently prepared and protected against light.

When irrigations are used, the agents and their strengths are as follows:

Strong protein silver, 1:2,000 to 1:1,000.
Mild protein silver, 1:1,000.
Potassium permanganate, 1:8,000 to 1:4,000.
Zinc permanganate, 1:8,000 to 1:4,000.
Acriflavine, 1:10,000 to 1:5,000.
Silver nitrate, 1:20,000 to 1:10,000.

Silver nitrate is not so well adapted for anterior as for posterior urethritis but is still used here by some urologists.

As the subacute stage arrives, intravesical irrigations of any of the milder antiseptic solutions are in order.

Nonspecific Anterior Urethritis.—Many of the same local antiseptics are useful in nonspecific infections of the urethra. Instillations of a 1 per cent solution of trinitrophenol have proved beneficial, from 5 to 10 drops being introduced gently into the urethra.

All the colloidal silver preparations find their indication here. The bladder should first be washed with 2 per cent boric acid solution, following which mild protein silver from 5 to 10 per cent or strong protein silver from 0.5 to 2 per cent should be used. Aqueous solution (from 3 to 5 per cent) of calcium chlorate or of resorcinol (0.25 to 1 per cent) is sometimes better than potassium permanganate or the silver salts for local treatment of uncomplicated pyogenic urethritis. They may be introduced either as irrigations or as instillations.

Another antiseptic of low toxicity and marked penetrating power is gentian violet medicinal, which is specific for staphylococcal infections. It may be introduced in 1 per cent solution into the urethra either by instillation or by irrigation. Mercurochrome from 0.25 to 1 per cent and metaphen in oil may also be used in these cases advantageously.

A part of the value of an irrigation is that it distends the urethra and so enables the medication to reach all parts of it. The complete filling of the urethra by a hand injection has a similar effect.

Posterior Urethritis.—In the acute stage of gonorrheal posterior urethritis no local treatment is given until irritant symptoms have subsided. In the subacute stage, urethrovesical irrigations of permanganate from 1:8,000 to 1:4,000 are given, or of silver nitrate 1:10,000. Another substitution recommended is that of zinc permanganate 1:8,000 to 1:4,000 as an irrigation. Deep instillations of silver nitrate 1:10,000 also give excellent results, carried out with the Guyon catheter. Strong protein silver from 5 to 10 per cent may be used if desired instead of silver nitrate.

CHRONIC URETHRITIS

In chronic urethritis silver nitrate has always been the mainstay of treatment. Irrigations with a 1:10,000 solution are useful, or deep instillations of from 0.5 to 2 per cent solutions. Any of the following may be used for irrigation:

Acriflavine, 1:10,000 to 1:5,000.
Mild protein silver, 1:400 to 1:100.
Strong protein silver, 0.25 to 0.5 per cent.
Potassium permanganate, 1:8,000 to 1:4,000.
Zinc permanganate, 1:8,000 to 1:4,000.

Urethritis in the Female.—In gonorrheal urethritis the same remedies are used as in the male, but they are applied by swabbing instead of by injections and are used in greater strength, from 1 to 10 per cent strong protein silver or from 0.5 to 2 per cent silver nitrate every second or third day. Potassium permanganate douches are given.

Nonspecific urethritis in women is usually called cystitis, and not without reason, since the infection is bound to reach the bladder. The term urethrocystitis has been suggested for the combined infection. The cause of this condition is nearly always traumatic. Instillations of mild protein silver from 5 to 10 per cent or of strong protein silver from 1 to 2 per cent afford some relief; mercurochrome from 0.25 to 1 per cent is also used here. Topical applications of silver nitrate from 5 to 75 per cent through the endoscope, although painful, serve to open up the ducts and allow the pent-up secretions to come away. They should not be repeated too often, however. Careful examination in these cases reveals that the primary inflammation is in the small posterior urethral glands. Instillations of mild protein silver from 10 to 50 per cent have also been found beneficial.

ACUTE CYSTITIS

In the most acute stage of cystitis, no local treatment is undertaken. A little later treatment with instillations of mild protein silver may be begun, from 25 to 50 per cent of the mild or from 1 to 2 per cent of the strong. Before instillation the bladder should be completely emptied by voiding, then irrigated with plain sterile water, hot boric acid solution or physiologic solution of sodium chloride. Another useful instillation is mercurochrome 1:100, left in the bladder as long as tolerated.

Bladder irrigations, also begun a little later, and preceded by lavage with boric acid or sterile water, may be done with any of the following:

Silver nitrate, 1:10,000 to 1:5,000.
Potassium permanganate, 1:8,000.
Acriflavine, 1:8,000.

Since silver nitrate is an irritant, its use should be preceded by as well as followed with application of a surface anesthetic such as metycaine. Such irrigations are useful in acute cystitis, provided there are no stones or malignant growths. The dyes may sometimes safely remain in the bladder for two or three hours. If the inflammation is due to some condition producing stasis, such as a stone or a tumor, local treatment will not correct it. Silver nitrate will sometimes clear up cystitis so effectively that its action appears almost to be specific. Since in the strength used (1:10,000) it is not an antiseptic, any action it exerts must be due to some reaction within the mucous membrane.

Nonspecific cystitis without renal or urethral involvement responds well to daily instillation of mercuriochrome from 0.5 to 1 per cent, especially in the female. In gram-positive infections of the bladder, irrigations of gentian violet from 1:10,000 to 1:5,000 or instillations of 1 per cent or more have a specific effect on the staphylococcus and certain other types of local infection.

CHRONIC CYSTITIS

In chronic cystitis the usual treatment is distention irrigation with silver nitrate from 1:10,000 to 1:1,000, after the bladder has been washed with a 2 per cent boric acid solution or distilled water; also instillation every other day of from 1 to 2 per cent silver nitrate, if not too painful. Otherwise, one of the silver proteins may be used. Potassium permanganate irrigations 1:8,000, used hot, are frequently beneficial. Mild protein silver from 10 to 15 per cent or strong protein silver from 0.25 to 2 per cent as an irrigation is widely employed. Some urologists still make use of mercury bichloride 1:30,000 for irrigation of the bladder. Mercurochrome 0.25 per cent and acriflavine from 1:10,000 to 1:5,000 are all used, and all give good results as irrigations in properly selected cases; 1:8,000 acriflavine dilutions have been found effective in bladder conditions secondary not only to acute gonococcal urethritis but also to nonspecific urethritis. The gravity method gives the best control of pressure when used with a blunt nozzle when this is practicable. While the chief purpose of bladder irrigations is a mechanical cleansing, the action of soothing medicaments on the bladder mucosa and the relief of tenesmus are also important objectives.

ACUTE PYELONEPHRITIS

In the very acute stage of infections of the renal pelvis, no local antiseptic treatment should be undertaken. Drainage by ureteral catheter is indicated, however, and when the inflammation becomes subacute pelvic lavage is of great importance to prevent chronicity. It is sometimes followed by dramatic improvement, which may be due to the action of the antiseptic employed but may be the result of improved drainage through mechanical dilation of the ureter. Before proceeding with kidney pelvis lavage, one should aspirate the contents of the pelvis. From 5 to 10 cc. of an antiseptic solution is then slowly injected and allowed to escape. Then more is injected and the process repeated a few times. The favorite lavage is done with silver nitrate 1 per cent. If this is too painful, as is often the case, some other substance of less irritating nature may be injected, such as mercuriochrome 1 to 5 per cent or gentian violet 1 to 5 per cent, the last named being used when the infective agent is gram positive. When the urine becomes clear these irrigations may cease.

Acriflavine 1:4,000 is an efficient antiseptic in the renal pelvis, but one must exercise due caution not to produce a chemical irritation of the mucous membrane. Irrigations of acriflavine from 1:10,000 to 1:4,000 may be alternated with irrigations of potassium permanganate 1:6,000 and mild protein silver 5 per cent.

CHRONIC PYELONEPHRITIS

In chronic pyelonephritis, renal lavage is the mainstay of treatment. The same general types of antiseptics are used as in subacute cases but not oftener than twice a week. It should be emphasized that when good results are observed it is a mistake to increase the dosage in the hope of still better results. On the contrary, excessive stimulation does harm, and the aim should be rather to decrease the amount of antiseptic gradually as the condition of the mucous membranes improves. After lavage of the kidney pelvis with silver nitrate solutions the mucosa is often found congested, its epithelium desquamated and a polymorphonuclear exudate present, giving evidence of an active inflammation. That this is an aid in eliminating a mild infection is borne out by numerous clinical reports. It is in this irritant or caustic effect rather than as an antiseptic that silver nitrate excels. One should take care that this caustic effect is not overdone. Experience and judgment are required to know when the chemical effect has reached the limit of the patient's tolerance. The course of treatment must often be protracted. Sometimes silver nitrate in 1 per cent strength achieves a lasting cure after one or two treatments, but often it has to be repeated once or twice a week for months. When there are no results, it is probable that the kidney substance is also involved along with the pelvis. In such cases from 3 to 5 cc. of a 1 per cent solution of mercuriochrome is often effective, since mercuriochrome has the property of penetrating rapidly through the tubules and cortical substance to the periphery of the kidney. Many subacute and chronic types of focal pyelonephritis respond satisfactorily to one form or another of lavage of the kidney pelvis. Formaldehyde 1:2,000 (in adults) and mild protein silver from 5 to 15 per cent have been credited with curative action.

SUMMARY

In combating infections in the urinary tract by means of antiseptic solutions applied locally (or topically) our purpose is twofold; namely, to destroy or at least retard the growth of specific invading bacteria and also to stimulate a reaction within the tissues involved so as to increase resistance at the site of the inflammation. It is not so much what particular agent is employed for this purpose as how it is employed. The clinician must ever be on guard against the use of antiseptic solutions so strong as to destroy the tissue he aims to preserve. He must remember that any substance sufficiently potent to kill bacteria outright also kills, at the same time, the tissue harboring those organisms. Only by employing the mildest solutions consistent with effectiveness can he hope for the desired results. Different persons react differently to particular medicaments. Youth will tolerate certain procedures that the aged patient, under no circumstances could endure. The personal equation should dictate in selecting and then perfecting oneself in one or two of the most popular local urinary antiseptics. It is better to know thoroughly the possibilities (and limi-

tations) of one or two of these agents than to use a score of them haphazardly. At best, this form of therapy is only an adjunct in the scheme of treatment; yet, when instituted with agents mild in their reaction, employed with the greatest gentleness and persisted in conscientiously, their place in urologic practice remains secure. Finally, and this urologists consider most important, self medication in the form of hand injections or irrigations, carried out by the patient himself, is to be emphatically discouraged.

Whitney Bank Building.

Council on Physical Therapy

THE COUNCIL ON PHYSICAL THERAPY HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORTS.

H. A. CARTER, Secretary.

S. O. S. OXYGEN THERAPY HUMIDIFIER ACCEPTABLE

Manufacturer: Oxygen Equipment and Service Company, 919 North Michigan Avenue, Chicago.

The S. O. S. Oxygen Therapy Humidifier is designed to humidify oxygen used in oxygen therapy by breaking the stream of gas into minute bubbles. According to the firm, this enables the oxygen to be more thoroughly saturated with water vapor than is possible with the ordinary wash-bottle humidifier.



S. O. S. Oxygen Therapy
Humidifier

The S. O. S. Oxygen Therapy Humidifier consists of a brass tube of heavy sheet metal, $3\frac{3}{16}$ inches in diameter, onto which is silver soldered a bottom and a heavy cast bronze top. On this top is silver soldered another brass tube 3 inches in diameter which hangs within three-sixteenths inch from the bottom. In the center of the head there is a heavy pipe which extends down close to the bottom. At the

lower extremity of this pipe there is a diffusion head which consists of several felt washers which are tightly packed. The oxygen is forced through these washers into the water, which breaks up the stream of oxygen into minute bubbles. These rise to the surface through one hole in the inside tube directly opposite the outlet. The oxygen must then flow around a space between the two tubes before passing through the outlet leading to the catheter. This (the firm states) very effectively traps any drops of water which might happen to be picked up.

A water level glass is mounted on the side of the unit and it is necessary to keep the level in sight at all times. The unit is filled through a petcock mounted on top of this glass. The petcock is opened and held to a flow of water. To empty, the petcock is opened and the unit turned upside down.

The firm states that the humidifier will produce from 80 to 90 per cent saturation of water vapor to the oxygen passing through. This permits pharyngeal insufflation over long periods of time without irritation to the mucous membranes in the nasal passages.

The S. O. S. Oxygen Therapy Humidifier was examined by an investigator acceptable to the Council. Tests were made to substantiate its stated efficiency as a humidifier. With regard to construction, it appeared to be substantially made.

The resistance in this unit is as follows: 4 liters, 58 mm. of mercury; 6 liters, 74 mm.; 8 liters, 82 mm.; 10 liters, 100 mm.

The absence of any sort of flow meter makes it undesirable to use this humidifier on an oxygen line but this is not important when the S. O. S. Oxygen Therapy Humidifier is used on large cylinders, as the reducing valve should be equipped

with a flow meter. A good flow meter does not appreciably change the rate of flow.

Method of testing: Oxygen was flowed through the unit at a fixed rate for six hours and the amount of water picked up by the oxygen was determined by weighing the humidifier before and after. The amount of water in each liter of oxygen was compared with the factor 0.022796 Gm., which is the amount of water vapor in one liter of oxygen 100 per cent saturated at room temperature. The efficiency varies somewhat with the rate of flow, the temperature of the room and the time the apparatus is used. If it is used for only a few minutes, there is more water picked up per liter than after the water becomes cold.

With 4 liters of oxygen for six hours the average humidity was 81 per cent.

With 6 liters of oxygen for six hours the average humidity was 66 per cent.

The humidifier furnished from 65 to 80 per cent humidity under ordinary conditions. It is not possible to say what the optimal humidity is for every patient. In conclusion, the investigator stated that the humidifier appears satisfactory at present.

In view of the foregoing report, the Council on Physical Therapy voted to include the S. O. S. Oxygen Therapy Humidifier in its list of accepted devices.

COMPREX CAUTERY, ANNIVERSARY MODEL, ACCEPTABLE

Manufacturer: Comprex Division, American Cystoscope Makers, Inc., 450 Whitlock Avenue, New York.

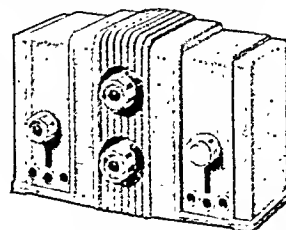
The Anniversary Model Comprex Cautery and Diagnostic Light is a small portable unit designed for cauterization purposes. It is similar mechanically to the Comprex Cautery and light transformer #201 (accepted, *THE JOURNAL*, May 31, 1930, p. 1760) but has a different housing which is claimed to improve its appearance and convenience. Accessories include a pistol-grip handle with spot light located above the tip and a choice of any of three standard tips. It comes in an ivory or black finish with ivory or green control knobs. The weight is approximately 5 pounds.

Simple operating controls are provided. The cautery and cautery light are connected to the machine by a single plug immediately beneath the on-off switch. Current intensity to the cautery is regulated by a five step control. There is a light regulator which is used both for cautery light and for diagnostic instruments. When the diagnostic light is employed, a double range current is available. The low range provides current for lamps up to 5 volt size; the high range permits utilization of 5 to 10 volt lamps. A single plug fits into the desired terminal outlet. If the diagnostic instrument employs an auto headlight bulb requiring very heavy current, it is plugged into the two outer "cautery" terminals. Then its brilliance is controlled by the cautery regulator instead of the light regulator. The unit operates on alternating current.

The pistol-grip handle, which is boilable, holds the cautery electrode at a comfortable angle for applications, according to the firm. It is also claimed that the small built-in headlight provides unobstructed illumination of the operating field. It is located above the handle but below the line of vision. Both the cautery and light are said to be shockproof and ground free, in addition to being individually regulated. The cautery tips are triply reinforced to guard against short circuiting.

The unit was investigated clinically and found to render satisfactory service. While the light is convenient for treating lesions in areas where intense illumination is required, shadows are not entirely eliminated.

In view of the foregoing report, the Council on Physical Therapy voted to include the Comprex Cautery, Anniversary Model, in its list of accepted devices.



Comprex Cautery

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

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SATURDAY, OCTOBER 15, 1933

AMERICAN HOSPITAL ASSOCIATION ESTABLISHES PRINCIPLES FOR MEDICAL SERVICE

At the annual session of the American Hospital Association recently held in Dallas, Texas, the following memorandum was prepared by the board of trustees of that organization and submitted to its house of delegates, which approved both the preamble and the conclusions.

CONCERNING THE PRINCIPLES OF RELATIONSHIP BETWEEN APPROVED HOSPITAL SERVICE ASSOCIATIONS AND THE MEDICAL PROFESSION IN PROPOSALS TO PRO- VIDE MEDICAL SERVICE ON AN INSURANCE BASIS TO HOSPITAL PATIENTS OF LIMITED INCOME

With more than 2,000,000 subscribers enrolled, and with membership increasing at the rate of more than one million per year, hospital service plans approved by the American Hospital Association are not only helping patients to pay their hospital bills, but are also contributing indirectly to the preservation of private medical practice in hospitals.

The prevalent restriction of these plans to semiprivate hospital service, and the omission of any provision for physicians' fees in hospital cases, have placed non-profit hospital care insurance beyond the reach of many employed workers of limited income.

There is a strong demand on the part of these low income groups for the creation of hospital service plans adapted to their means. Medical societies are now studying, and in some cases are preparing to sponsor, group payment plans to cover medical fees of patients of limited means. If these efforts are successful, they will reclaim for private medical practice a segment of medical service in hospitals even larger than that which is protected by existing hospital care insurance plans.

The American Hospital Association believes that efforts by the local medical profession to extend the voluntary insurance principles to medical fees in hospital practice can be assisted by cooperation with approved hospital care insurance plans. Approved plans are urged to offer their cooperation and assistance to this end. Joint efforts will make hospital care available to millions of persons of limited means, who in this manner would pay for both hospital care and medical treatment in hospitals.

The American Hospital Association is prepared to approve periodic payment plans for hospital care and medical service in hospitals which are also approved by the local medical profession and which conform to the following principles:

1. Sponsorship and control by non-profit organizations, representative of hospitals, the medical profession, and the public.

2. Free choice of physician and free choice of hospital consistent with existing relations between approved hospitals and their physicians.

3. Financial soundness and adequate accounting.

4. Equitable payments to physicians and to hospitals.

5. Separate finances and reserves for hospital care and for medical services of attending physicians.

6. Hospital and medical service benefits determined by hospitals and the local profession.

7. Dignified promotion and administration.

The American Medical Association is invited to confer with the American Hospital Association regarding these and related problems with a view to harmonious joint action in the public interest.

Thus the American Hospital Association indicates a willingness to cooperate with the American Medical Association with a view to harmonious joint action in the public interest. It recognizes the right of the physician to control the terms of his service. It recognizes the free choice of physician and free choice of hospital as fundamental to good medical care. It supports the established action of the House of Delegates of the American Medical Association in maintaining separate finances and reserves for hospital care and for the service of the physician.

It is encouraging to have such a statement from the leaders in the field of the hospital, since the hospital is today a center of medical service. The action taken by both the American Medical Association and the American Hospital Association now permits the establishment of cooperative plans for group payment for medical service without invalidating any of those ideals or principles associated with medical care which are vital to the provision of good medical service.

HIPPURIC ACID TEST AS AN INDEX OF HEPATIC DAMAGE

Since the classic investigations by Bunge and Schmiedeberg in 1877 it has been believed that synthesis of hippuric acid takes place in the kidney exclusively. More recent researches make it appear that this synthesis, at least in man, takes place in the liver as well. The conjugation of benzoic acid with aminoacetic acid to form hippuric acid represents one of the several mechanisms by means of which the liver detoxifies certain noxious substances brought to it from the gastrointestinal tract. Quick¹ found that the excretion of hippuric acid proceeded at a constant rate regardless of the amount of sodium benzoate ingested but that such excretion could be greatly increased by the ingestion of aminoacetic acid. He concluded, therefore, that the quantity of hippuric acid excreted per hour represented the maximum capacity of the organism to synthesize aminoacetic acid. Since aminoacetic acid is said to be formed in the liver, diminution in the output of hippuric acid would seem to indicate a

1. Quick, A. J.: The Synthesis of Hippuric Acid: A New Test of Liver Function, *Am. J. M. Sc.* 185: 630 (May) 1933.

lowered hepatic function due to certain types of hepatic damage.²

Quick found in a series of clinical cases that the synthesis of hippuric acid was strikingly diminished in catarrhal jaundice, in syphilitic cirrhosis and in obstructive jaundice of moderately long duration. He concluded that the test offers an approximate quantitative measure of liver damage and that it is a valuable aid in the diagnosis of liver diseases.

Boyce and McFetridge³ in recent contributions emphasize the role of the liver in biliary surgery and its heretofore but little recognized importance in thyroid disease as well as in a number of various surgical diseases. Dinsmore, Lahey, Weller, Beaver and Pemberton, among other workers, pointed out the association of damage to the liver with toxic disease of the thyroid. Lahey stated that the postoperative thyroid crisis was in reality hepatic failure and that the deaths associated with hyperthyroidism were "liver deaths." Bartels of the Lahey Clinic and Boyce and McFetridge utilized the Quick test for determination of the amount of hepatic damage in thyrotoxic cases. Boyce and McFetridge believe that by the application of repeated tests they can safely say at the end of the planned preparation that the patient has become a good risk as far as the liver is concerned, or has become a fair one, or remains a poor one and must be further prepared in anticipation of the drop in hepatic function which their experience with the test indicates may follow any surgical procedure. The practical application of the knowledge thus obtained has been to stress the value of intravenous dextrose therapy as prophylaxis against the thyroid crisis.

Boyce and McFetridge studied as controls a group of presumably normal persons who were to undergo elective operations for conditions not connected with the biliary tract or the thyroid gland. In all cases there was a definite drop in hepatic function after operation, the impairment being most marked with spinal analgesia and least marked with ethylene anesthesia. They are convinced that the Quick test offers a more delicate index of hepatic function than either the bilirubin test or the dye test.

2. In the Quick test for hepatic function 5.9 Gm. of sodium benzoate dissolved in 30 cc. of water is administered one hour after a breakfast consisting of coffee and toast. The patient is then given half a glass of water. Immediately after taking the drug the patient urinates and then collects complete hourly specimens for four hours. These are preserved with toluene, and the hippuric acid content is determined in each specimen. In normal adults the output of benzoic acid, as hippuric acid, is approximately 1 Gm. or more during the second and third hours, and the total for the four hours is from 3 to 3.5 Gm. The estimation of the hippuric acid for clinical purposes is accomplished by transferring to a small beaker each hourly specimen, which is measured and is acidified with concentrated hydrochloric acid to congo red. The solution is vigorously stirred until the precipitation of the hippuric acid is complete and then is allowed to stand for one hour at room temperature. The precipitate is filtered off on a small Buchner funnel or a filter plate, washed with a small quantity of cold water and allowed to air dry. The hippuric acid thus obtained is either weighed or titrated with 0.2 normal sodium hydroxide, phenolphthalein being used as indicator. To obtain the total hippuric acid content one must add to the amount thus obtained the calculated quantity remaining in solution; 100 cc. of urine will dissolve 0.33 Gm. of hippuric acid. In case any specimen exceeds 125 cc. it should be slightly acidified with acetic acid and concentrated on the water bath to about 50 cc. before the hippuric acid is precipitated.

3. Boyce, F. F., and McFetridge, E. M.: Studies of Hepatic Function by the Quick Hippuric Acid Test: I. Biliary and Hepatic Disease, *Arch. Surg.* 37:401 (Sept.) 1938; II. Thyroid Disease, *ibid.* p. 427; III. Various Surgical States, *ibid.*, p. 443.

The author of the test suggests that vomiting when the test is applied to toxic patients may be a disadvantage. Another disadvantage is that the test cannot be applied in cases of nephritis with nitrogen retention. Quick believes that the well known objections levied against the inadequacy of every liver test do not hold in his case. He believes that certain mechanisms of the liver are so delicate that there is practically no margin of safety. He points to the reduction in the excretion of hippuric acid in catarrhal jaundice, which is out of all proportion to the amount of structural change observed in this disease, as a proof that the mechanism concerned with the synthesis of aminoacetic acid has little reserve. The objection that the test measures only one function of the liver is met by the argument that the various functions of the organism are closely interrelated so that an injury to any one mechanism is apt to affect several others as well. According to Mann, however, conclusive proof is not available to show that the liver is the sole site of the synthesis of hippuric acid. Mann further emphasized that it would be important to study the test in relation to the physiologic state of the liver as well as to have more information with regard to the rate of elimination of hippuric acid in the toxic nephroses which are frequently associated with hepatic damage.

DISABILITIES AMONG EMPLOYEES OF A PUBLIC UTILITY

The study of disabilities among employees of specific industries is contributing information which should be helpful not only to the industrial physician but also to the general problem of disease control and to the formulation of specific preventive and ameliorative measures. Gafafer and Frasier¹ studied disability among employees of the Boston Edison Company as represented by absences due to disabilities lasting one calendar day or longer during 1933 to 1937 inclusive. The causes of disability are broadly grouped into industrial accidents, nonindustrial accidents, respiratory diseases and nonrespiratory diseases. There were altogether 16,241 total years of exposure with 17,628 absences lasting one calendar day or longer over the five year period. These absences totaled 133,022 days of disability. The frequency of absences by years showed a practically stationary trend for both males and females, the trend for the former being on a lower level.

The yearly rate for industrial accidents among male employees since 1934 has shown a decidedly downward time trend and a slightly lower trend for nonindustrial injuries. For the entire period the annual number of days of absence per person for all disabilities was 7,518 for males, with an average number of days per absence of 8.35 for the entire period. The corresponding rates for women were 10,855 and 5.96 respectively. The

1. Gafafer, W. M., and Frasier, Elizabeth S.: Frequency and Duration of Disabilities Causing Absence from Work Among the Employees of a Public Utility, 1933-1937, *Pub. Health Rep.* 53:1273 (July 29) 1938.

diseases and conditions which caused the largest number of days of disability per male employee were "influenza and grip" 1.2 days, "nonindustrial injuries" 0.6 days, and "all other diseases and conditions" 1.2 days. The largest annual number of days of disability for females were due to "influenza and grip" 1.7 days and to "all other diseases and conditions" 1.4 days. Among the male employees the shortest average duration per absence is shown for "colds and coryza," 2.8 days, and the longest for "industrial injury," 28.5 days.

Remarkable differences are shown in the duration of disability in calendar days for the two sexes. For all disabilities the one day absences among women were nearly three times as numerous as among men, while two day absences were twice as frequent. One day disabilities due to nonrespiratory and nondigestive diseases occurred more than seven times as often among the females as among the males; this difference cannot be explained entirely by the presence of dysmenorrhea, since disregard of absences caused by this condition indicates a frequency among the females still four times as great as that among the males. The differential did not hold proportionately for absences of longer duration, since only 205.6 absences per thousand males and 313.6 absences per thousand females extended through the seventh day. Within this one industry there was a wide variation in frequency of absences. The highest rates during the period among male employees were shown by linemen, followed by meter readers, repairmen, helpers and chauffeurs. Trouble men, engineers, division heads and station operators had comparatively low rates of absences due to disability. Among women, office cleaners averaged approximately three absences per person annually and the rate for female clerks was almost twice the rate for male clerks. Telephone operators among women experienced a slightly lower rate than male telephone operators. Approximately 45 per cent of the days of disability among the men occurred during the first seven days after onset and for women the corresponding percentage was 52.

This study was made possible by the fact that in 1913 the company inaugurated a liberal disability benefit plan which provided for payment of wages in full or in part during disability, beginning with the first day of absence. During the second six months of membership, an employee is allowed accumulated sick leave of one day a month at full pay. After the first year of membership, full pay for continuous disability is allowed for fifteen weeks; beyond this time from three fourths to one fourth of the employee's wages are paid, the period of payment depending on the number of years of employment with the company.

Perhaps the most important feature of this report is the fact brought out that 45 per cent of disability among men and 52 per cent of disability among women is of less than seven days in duration. Nearly half of the disabilities are therefore so brief, relatively speaking,

that with rare exceptions the economic burdens which they produce could be carried relatively easily either by the employee alone or by the company alone. Judging from this experience, it would be the other half in which illnesses exceeding one week in duration and especially when extending into further weeks, months or years that must inevitably cause the greatest economic strain on an individual, his family, the company and the public. Might it not, therefore, be more advisable to exempt the first one, two or even three weeks of disability from sick benefits and to employ the savings toward the protection of those who may be faced with more serious hardship? Sufficient information should now be available in many industries so that such a modification could be studied and possibly placed into effect exempting the relatively benign disabilities from benefits and concentrating on those which are truly economically crippling.

Current Comment

HEIGHT OF AMERICAN WOMEN

The common impression that the typical American woman has been growing taller has been subjected to a recent brief analysis.¹ Women accepted for "standard" insurance by the Metropolitan Life Insurance Company between 1922 and 1934 showed an average height (with shoes) of 5 feet 4½ inches (162.7 cm.) in middle adult life when full growth had been attained. This figure is identical with that obtained in two earlier life insurance studies based on the material of several companies covering the years 1885-1908 and 1909-1927. There is, however, some evidence that women in the younger ages insured in 1932 and 1935 had a greater average height than those insured in 1920-1923, so that future averages may change. Although these "averages" argue against an increase in height in recent years, they are not in conformity with the observations of Bowles on the heights of college graduates of four women's colleges, or the studies at Stanford University and Barnard, which do indicate an average increase in height for college women. This apparent discrepancy may be explained, perhaps, by differences in the race stocks which make up the populations in question. The average heights are generally greater for western European stocks than for southern and eastern European stocks. Since there has been a definite change in the proportions of various stocks composing the population in the last fifty years, with an increasing proportion of persons from the shorter ones, the life insurance figures may have been affected by this factor. The sharp curtailment in immigration during and after the war with the reduction in number of shorter foreign born women and the intermingling of racial types will probably tend to overcome the effect of this factor. Hence it is likely that in the course of a generation the average height of women in the population as a whole will show a substantial increase paralleling to a greater degree that already shown by studies of women in college groups.

1. Is the Average Height of American Women Increasing? Statistical Bulletin, Metropolitan Life Insurance Company 19:3 (Aug.) 1932.

ORGANIZATION SECTION

PRESS COMMENT ON THE SPECIAL SESSION OF THE HOUSE OF DELEGATES

The special session of the House of Delegates of the American Medical Association developed some specific conclusions regarding the future trend in medical practice and also in relationship specifically to the National Health Program. The reactions of the press of the country to these decisions of the House of Delegates should interest every physician. In general, comments were highly favorable to the American Medical Association. Thus the Cincinnati *Star* said:

The attitude of the A. M. A. toward what is loosely called "socialized medicine," should be clearly understood. Its first concern has been to safeguard the standards of private medicine in order to protect the public health. It has insisted upon the right of the patient to select his own physician. It has opposed the hiring of physicians either by private groups or by the government. It has always opposed, and its house of delegates opposed again at Chicago, the New Deal proposal for a compulsory health insurance tax because such taxation would lead to political control and manipulation. At the same time, it now realizes that private medicine, while preserving intact its traditional standards, must exert all its energy and ingenuity to meet the demand for more adequate medical care for the masses of the people.

In the past the A. M. A. has been on the right side but has not always made its point of view clear to the public. The Chicago meeting should be the beginning of a new era, in which the medical profession will show that its opposition to state medicine and to any outside control of medicine is based not on self-interest but solely on solicitude for the public health.

The Detroit *News* sees a trend toward liberalism:

Organized medicine, nationally and in Michigan, through the house of delegates of the American Medical Association and the similar body representing the Michigan Medical Association, has materially modified its former stiff opposition to extension of medical facilities under Government auspices. . . . A medical departure in the direction of liberalism is reflected, we think. Acting unanimously, the physicians show themselves responsive to conditions which have been under study for years. A striking fact the studies developed is that, while needs for their services were shown, thousands of capable doctors do not find employment enough to return them a decent living.

The Chicago *Drovers' Journal* fears the entrance of politics into medical care:

There are plenty of arguments for and against the proposition of federal medical service, but it all simmers down to whether or not the service is well administered and not permitted to fall into the hands of the politicians. We are all familiar with the way all kinds of service deteriorates when the spoilsman secure control and this seems to be the chief danger. No reputable and conscientious physician wants to see his profession dragged into the mire of politics.

Medical service is one of the most important and necessary services rendered to mankind and whenever it is socialized or regimented, it becomes more or less subject to political influences. It is the poor people who would suffer rather than benefit from political practitioners.

The Indianapolis *News* commends the fair solution of the problem reached by the House of Delegates:

The resolutions adopted by the house of delegates of the American Medical Association, which met at Chicago in special federal public health plan, testify at once to the willingness

of physicians to make the sacrifices for which their profession is notable and to engage in a political contest for the preservation of their integrity and the welfare of all the people who are in need of medical attention. They declared positively against federal compulsory sickness insurance. This plan would call for a tax on pay rolls and the use of the money to finance medical attention, under political control, for the insured people. It would subordinate the doctor to the politicians and it might even involve the forcing of doctors to prescribe medicines and treatments controlled by politicians. The final effect might be to victimize the sick and enrich the politicians at their expense. . . . The delegates, representing the 110,000 members of the association, have offered a fair solution of this important problem. Their resolutions imply a fundamental interest in the health of the people and the protection of the sick from political exploitation.

The comment of the Indianapolis *Star* was:

The general aim of the American Medical Association is to help the citizens to help themselves. Government subsidy of control over group hospitalization plans is opposed. The country, furthermore, does not need and should not want a complicated, bureaucratic political system of dealing with medical care. All who need attention should have it but that care should not be made the pretext for regimenting as well as expending the public health service.

In Florida, the Miami *Herald* commented:

The trend of the times has been to some sort of socialized medicine. The *Herald* neither approves nor condemns the theory. But it has felt the medical profession owed it to itself to guide the movement, and not let it become the tool of politicians to the detriment of the doctors and to the damage of the masses whom it purports to protect.

In Paducah, Ky., the *Sun Democrat* appreciates the physician's point of view:

Representatives of the American Medical Association meeting in Chicago to diagnose the medical requirements of the needy prescribe among other things that additional hospital facilities be utilized more fully, that a greater degree of public aid for medical care be extended the under privileged, and that compulsory health insurance be avoided as injurious to the body politic.

The recommendations are constructive. They represent the considered judgment of experts in consultation on a problem with which they are thoroughly familiar by virtue of first hand experience. . . .

The relationship between the doctor and his patient is a highly personal one. Curing the sick is not a cut and dried matter like painting a house or driving an automobile. Scientific knowledge is required, of course; but so, too, are tact, patience, psychology, and fortitude on both sides. Doctors realize this better than anyone, and they are quick to resent outside interference from any source.

In Youngstown, Ohio, the *Vindicator* said:

The points of agreement are so many and cover so wide a field that they offer a basis of cooperation which probably will satisfy most laymen. It will be better to proceed on that basis, for the present at least; if the changes which the A. M. A. approves work well enough to indicate that a still further extension of government aid in the health field is desirable, it will come inevitably. Meanwhile the government will have the cooperation of the medical profession, without which no public health plan can be wholly satisfactory.

For a time a too conservative leadership in the A. M. A. undermined public confidence in the organization. Considering

the present evidence of a profound change in the medical attitude toward public health, the people probably will be willing now to put at least as much faith in the advice of their doctors as that of their politicians. The government should go forward on the basis provided by the association's very liberal concessions, and leave more sweeping changes to a time when further experience with "socialized medicine" has made the proper path clearer.

In Cleveland the *Plain Dealer* said in an editorial which was widely copied:

By its action Saturday at Chicago the house of delegates of the American Medical Association goes a long way to refute the criticism, heard in many quarters, that the association in its zeal to protect existing professional methods, ignores the plight of a vast number of Americans who now lack adequate medical service because they can not afford to pay for it at the going rates. . . .

The New York *Times*, as might have been anticipated, conceded in a grumbling manner that progress had been made toward a liberal attitude on the part of the House of Delegates of the American Medical Association. The *Times* said under the heading "Medicine Steps Forward":

Both physicians and the public cannot but approve the decision of the House of Delegates of the American Medical Association to recede from its previous position and, on the whole, to endorse the Government's program with the exception of the provision for compulsory health insurance. Hospital insurance of the three-cents-a-day type, cash indemnity insurance which is supposed to meet the heavier costs of serious illness, the expansion of workmen's compensation laws to cover occupational ills, the utilization of Federal and State funds to bring medical care to the indigent—these proposals, once repudiated, are now apparently accepted in principle. Even more important is the obvious willingness of the Association to assume the lead in laying down the new health policy and an implied intention of doing what it can to keep politics out of the kind of medical care that the poor are to receive.

Gratifying as this progress may be, crucial issues are still untouched. The plight of the class that barely earns enough to pay for food, shelter and clothing and has nothing left over wherewith to pay the doctor will undoubtedly be relieved. What of the many who cannot pay even reduced physicians' fees but can set aside regularly something for medical treatment? They must turn to the public hospitals or private charity. Yet the Association advocates more efficient use of

existing hospital facilities in one breath and in another illegally insists that hospitals should not provide medical care. Moreover, workmen's compensation is to be expanded to include sickness benefits, but employers and employees must have nothing to do with salaried or contract medicine.

The public is waiting for a plan which will enlist all voluntary agencies in coping with the problem of illness before taxation is invoked. Cooperatives, clinics of the Mayo and the hospital type where physicians practice in groups, contract medicine whereby physicians on a salary or higher compensation basis are enabled to minister to the sick employees of a manufacturing company can be very effective. Must experimentation in these democratic directions still struggle under legal disabilities largely of organized medicine's creation? More concessions must here be made before the country will be convinced that the need of taxation has been reduced to an inescapable minimum.

Obviously, the editorial writer for the New York *Times* is still uninformed as to the basic requirements for good medical practice.

The Washington, D. C., *Post* said:

The A. M. A. did not withdraw its objections to cooperative health associations. On the contrary, its resolution says: "Experience in the operation of hospital service insurance or group hospitalization plans has demonstrated that these plans should confine themselves to provision of hospital facilities and should not include any type of medical care." That statement leaves much to be desired. Yet it is obvious from the more positive resolutions adopted that the A. M. A. as well as many individual doctors are taking a more liberal view of the profession's obligation to society.

That fact stands out more significantly than any other development at the delegates' emergency meeting in Chicago. The urgent need for more adequate medical care within the lower income groups is not open to question. If that deficiency is to be corrected full cooperation of the organized medical profession is certainly essential. Indeed, leadership of the movement by the profession may afford the only assurance of continued progress.

If the Administration is wise, therefore, it will welcome the concessions made by the governing body of the A. M. A. and attempt to extend the area of cooperative effort for better public health. The association made a serious mistake when it set out to undermine cooperative health experiments. But that mistake is not likely to be corrected by prosecution of the Medical Association under the anti-trust laws. Even if the courts could be convinced that this professional organization is restraining "trade," it is doubtful whether the result would be constructive.

MEDICAL ECONOMIC ABSTRACTS

SICKNESS UNDER NATIONAL HEALTH INSURANCE

At the health congress of the Royal Sanitary Institute, July 11 to 16, 1938, Dr. A. B. Walker, Regional Medical Officer of the Department of Health for Scotland, discussed "The Duration of Incapacitating Sickness" under national health insurance. He summed up much of the material covered in his paper in the following early paragraph:

"The National Health Insurance Act was designed principally as an instrument to improve the standard of curative medicine in general practice by replacing the old club system of contract practice. It was reasonable to hope that this act, together with the improved environmental services, by providing early and effective treatment would have some effect not only in diminishing the amount and duration of disabling illness but also an important preventive element. Yet, whilst sickness insurance on a national scale is a social service of proved value, it has not had these effects. Morbidity data available during the past few years show that incapacitating illness has tended to rise and with yearly fluctuations remains today at a new high level. This

persistence of incapacitating illness amongst the insured population at a high general level, in spite of advances in preventive and curative medicine, is indicated in the successive Annual Reports on Incapacitating Sickness in the Insured Population, published by the Department of Health for Scotland. It is a fact which deserves the serious consideration of all interested in the public welfare."

In the year 1935-1936 "the number of days of incapacity for an insured person per annum" was 11½ days, "an increase of 5 per cent over the previous year," which constituted a "new high record." (This, incidentally, is a higher figure than any of numerous "surveys" that have been conducted in the U. S. have been able to discover.) Yet the insured population excludes young children and all persons over 65 years of age. The average duration of individual sicknesses has increased from a quinquennial average, in the years 1930-1935 inclusive, of 46.66 days to 52.1 in 1935 and 1936. While the figures for 1936-1937 have not yet been published, Dr. Walker states: "I am informed that they show no evidence of any general improvement. They are, in fact, in some respects the worst noted since these data were first recorded seven years

ago." Part of this is due to an influenza epidemic but the upward trend would have continued even without this exceptional condition.

He does not apparently consider that this sickness is due only to a lack of medical attention but rather asks the question "whether further and more intensive efforts to improve environment are required in the direction of housing, reduction of overcrowding, instruction in personal hygiene, eradication of bad dietetic and other habits, etc." He also recognizes that there is a question of whether this has been due "to a real increase in incapacitating sickness" or "to an increase in payments to persons who are not, in fact, incapable of work." He notes that there was a "tremendous rise in payments in 1926 at the time of the general strike, when there were no outbreaks of epidemic disease." He also suggests that "too great a concentration by the patient on the efforts and means to cure him sometimes results in prolonging his illness." There has been an apparently great increase in psychoneurosis, although he mentions that this may possibly be due to an increased tendency among physicians to emphasize such illnesses. A test of thirty-four insulin-treated diabetic patients "showed that the facilities available for supervision and treatment were inadequate and that in the majority of cases the disease was not properly controlled" and complains that "there is a vast lag between present-day knowledge of preventive medicine and the practical application of this knowledge in family practice." Even under insurance, medical facilities "should be made use of at a relatively earlier stage in the development of illness."

CARE FOR SOCIAL SECURITY CLIENTS IN THE STATE OF WASHINGTON

The State Department of Social Security of Washington has approved a plan for medical-dental care which is based on the one previously in effect under the Federal Emergency Relief Administration and follows closely plans submitted by the Washington State Medical Association and by the State Dental Association. The plan is in line with the following resolution passed by the Washington State Association of County Commissioners in their annual meeting held in Yakima from June 24 to 26, 1937:

WHEREAS, It is the desire of the county commissioners of the state of Washington to extend the best possible medical service consistent with funds available to the people of the state of Washington who must depend on public support for such services;

WHEREAS, Our principles of American liberty and independence dictate that such service should include a free choice of physician; and

WHEREAS, The State Social Security Act provides funds for medical services and empowers the several boards of county commissioners to contract for such services; be it

Resolved, That we, the Washington State Association of County Commissioners, endorse the adoption by county boards of medical programs which provide for contracts with and between their local medical and dental profession adapted to local conditions and granting free choice of physician.

A State Medical-Dental Board has been set up "to be composed of one or more but not to exceed three representatives of the Executive Board of the State Association of County Commissioners, the State Director of Health, the State Directory of Social Security, a committee of three physicians elected or appointed by the Washington State Medical Association or its duly authorized agency, and three dentists elected or appointed by the Washington State Dental Association."

A County Medical-Dental Board has been created in each county, "to be composed of three County Commissioners, the County Health Officer, Local Administrator for Public Assistance, a committee of three physicians elected or appointed by the County Medical Society, and three dentists elected or appointed by the County Dental Society." The doctors and dentists are to be appointed by the respective county medical-dental groups and are generally to "supervise and administer the medical-dental program of its respective county." The duty is placed on the county board of undertaking "as its immediate responsibility a study of medical-dental service in the county over the past three or four years," of drawing up a plan for medical-dental care, and of recommending "an amount monthly and quarterly to cover medical-dental care."

Any licensed physician or dentist who agrees to abide by the rules and regulations shall be entitled to practice under the agreement and be subject to the free choice of the patients covered. The procedure under the plan as outlined is much like that under the FERA, except that it provides for practically all forms of medical care, including separate agreements for hospitalization. What might be called a standard fee schedule is established but it is provided that this "shall be subject to prorating in keeping with the budgeted funds avail-

Fee Schedule

First office or home visit.....	\$ 3.00
Subsequent home visits.....	2.50
Subsequent office visits.....	2.00
Obstetric Care: Antepartum on per call basis but not to exceed the maximum of.....	10.00
Delivery (when in the home) including postpartum care.....	20.00
Delivery (when in the hospital or maternity home) including postpartum care.....	10.00
Fractures and dislocation cases shall be at the State Department of Labor and Industries rates.	
X-rays (when authorized by the Medical Executive Committee) shall be at the State Department of Labor and Industries rates.	
Eye examinations (refractions and subsequent check up).....	5.00
Special physical examination or special examination by a psychiatrist in certain child welfare cases (not subject to prorating).....	3.00
Requisition must read "special—not subject to prorating."	

able for the Medical-Dental Program for the county." This fee schedule covers the items given in the accompanying table.

Special operative procedures where included shall as nearly as possible be billed to conform to the State Department of Labor and Industries fee schedule. (Subject to change and adjustment of the State Medical-Dental Board.) Only one call will be allowed regardless of the number of patients seen in a family on the same visit.

Fifty cents per mile one way from beyond the city limits will be allowed per trip irrespective of the number of homes or patients visited, except that no mileage shall be allowed on the first three miles from the city center.

Fees for all services shall be subject to the approval of the State Medical Executive Committee.

There are separate provisions for the dentists describing the character and limits of the service to be given and for a county medical-dental board to examine the work done and to authorize payment.

PAYMENT FOR PHYSICIANS' SERVICES IN OUTPATIENT DEPARTMENTS

New York physicians are seeking to obtain payment for physicians in dispensary service. The Commissioner of Hospitals, Dr. S. S. Goldwater, has agreed that dispensary physicians

Percentage of Population Treated in the Outpatient Departments of Hospitals in Greater New York

Years	Population of Greater New York*	Number of Outpatient Department Patients†	Per Cent of Population Treated in Outpatient Department	Per Cent on 4.5 Visits
1920.....	5,686,249	927,421	16.3
1929.....	6,881,882	1,632,937	24.0
1930.....	7,014,619	1,874,750	26.7
1931.....	7,090,069	2,020,580	28.6	19.1
1932.....	7,218,223	2,229,405	30.9	20.6
1933.....	7,346,007	2,279,307	31.0	20.7
1934.....	7,473,791	2,328,672	31.1	20.5
1935.....	7,294,894§	2,356,631	32.3	21.5
1936.....	7,362,624	2,372,566	32.2	21.5

* Bureau of Vital Statistics—Department of Health. In 1935 known as the Bureau of Records of the Department of Health.

† Figures do not include patients treated in dispensaries not connected with hospitals.

‡ This figure obtained by dividing the number of visits to the outpatient department by 3.

§ Estimated by a new method by the Bureau of Records adopted by the Federal Bureau of the Census.

should be paid and will incorporate the necessary amount to do this in his budget. According to the *New York Medical Week* (17:3 [Aug. 27] 1938) there is still little hope that the necessary appropriation will be made.

There has been such a steady increase in the number of persons and the percentage of the population treated in outpatient departments as to make this form of practice a formidable competitor of private practice and to constitute a heavy burden on the physicians who give their services without pay.

OFFICIAL NOTES

SCIENTIFIC EXHIBIT

Application blanks are now available for space in the Scientific Exhibit at the St. Louis Session, May 15-19, 1939. Attention is called to the fact that the meeting is a month earlier than usual, and applications close Jan. 5, 1939. Blanks will be sent on request to the Director, Scientific Exhibit, American Medical Association, 535 North Dearborn Street, Chicago.

RADIO BROADCASTS

The fourth series of programs broadcast in dramatic form portraying fictitious but typical incidents of significance in relation to health by the American Medical Association and the National Broadcasting Company entitled "Your Health" will begin Wednesday, October 19, and run consecutively for thirty-six weeks. The program will be broadcast over the Blue network of the National Broadcasting Company each Wednesday at 2 p. m. eastern standard time (1 p. m. central standard time, 12 noon mountain time, 11 a. m. Pacific time).*

These programs will be broadcast on what is known in radio as a sustaining basis; that is, the time is furnished gratis by the radio network and local stations and no revenue is derived from the programs. Therefore, local stations may or may not take the program, at their discretion, except those stations which are owned and operated by the National Broadcasting Company.

The programs to be broadcast in the first group, together with their dates and their topics, are as follows:

October 19. What Is Health?
October 26. Growing Strong.†
November 2. Seeing and Hearing Well.
November 9. Healthier Boys and Girls.

The following is a list of the stations connected with the Blue network of the National Broadcasting Company, but no assurance can be given as to how many of these stations will broadcast the program "Your Health":

Basic Blue Network					
WJZ	New York	WEBR	Buffalo	KSO	Des Moines
WBZ	Boston	KDKA	Pittsburgh	KOIL	Omaha
WBZA	Springfield	WHK	Cleveland	WREN	Kansas City
WEAN	Providence	WSPD	Toledo	WLW	Cincinnati
WICC	Bridgeport	WXYZ	Detroit	WCKY	Cincinnati
WFIL	Philadelphia	WOWO	Fort Wayne	WSAI	Cincinnati
WBAL	Baltimore	WENR-WLS	Chicago*	WRTD	Richmond
WMAL	Washington	KWK	St. Louis	WABY	Albany
WSYR	Syracuse	WMT	Cedar Rapids	WJTN	James't'n, N.Y.
WHAM	Rochester	WTCN	Minneapolis-St. Paul	WLEU	Erie

Supplementary Facilities					
WFEA	Manchester, N. H.	WFBC	Greenville	KVOD	Denver
WBRE	Wilkes-Barre	WWNC	Asheville	KLO	Ogden
WSAN	Allentown, Pa.	WIS	Columbia	KIDO	Boise
WORK	York, Pa.	WCSC	Charleston	KGIR	Butte
WCOL	Columbus, O.	WJAX	Jacksonville	KPFA	Helena
WGL-WOVO		WFLA-WSUN	Tampa	KGHL	Billings
		WIOD	Miami	KSEI	Pocatello, Ida.
	Ft. Wayne	WMC	Memphis	KTFI	Twin Falls, Ida.
WOOD	Grand Rapids	WSB	Atlanta	KGO	San Francisco
WBOW	Terre Haute	WBRC	Birmingham	KECA	Los Angeles
WGBF	Evansville	WJDX	Jackson	KEX	Portland, Ore.
WEBC	Duluth-Sup'r'r	WSMB	New Orleans	KJR	Seattle
KSOO-KELO		WALA	Mobile	KGA	Spokane
	Sioux Falls, S. D.	WROL	Knoxville	KFBK	Sacramento
KANS	Wichita	WAVE	Louisville	KWG	Stockton
WTAR	Norfolk	WSM	Nashville	KMJ	Fresno
WPTF	Raleigh	WTMJ	Milwaukee	KERN	Bakersfield
WSOC	Charlotte	WTBA	Madison		

* Owing to program conflicts, there will be no Chicago broadcast of the network program. Instead, a recording of the program will be broadcast over Station WENR at 8 p. m. each Wednesday. This recording will be an identical rebroadcast of the network program broadcast earlier the same day.

† Program may be cancelled; attempting to arrange an evening program.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ALABAMA

Personal.—Dr. William Bruce Nelson, Fairfield, has been appointed health officer of Baldwin County to succeed Dr. Arthur J. Vandergrind, Bay Minette, who has accepted a commission in the U. S. Army Medical Corps.—Dr. Hugh C. McRae, formerly health officer of Lee County and recently engaged in special work under the supervision of the bureau of preventable diseases of the state department of health, has been appointed health officer of Marion County, effective September 15, succeeding Dr. Thomas L. Owings, Hamilton, resigned.

CALIFORNIA

Plague Infection.—According to *Public Health Reports*, plague infection was proved in one fisher squirrel collected July 20, 6 miles east of Seven Oaks, San Bernardino County, and in a pool of eighty-four fleas collected August 8 from fifty-two fisher squirrels from the Crestline public dump, 2 miles northeast of Crestline, San Bernardino County.

Program on Sulfanilamide.—The San Francisco County Medical Society devoted its meeting October 11 to a discussion of sulfanilamide. The speakers included Drs. Windsor C. Cutting, chemistry and pharmacology; Arthur Haim, experimental background; Arthur L. Bloomfield, use in internal medicine; Edward B. Shaw, use in pediatrics; Donald A. Dallas, use in gynecology and obstetrics, and Clark M. Johnson, use in urology.

COLORADO

Personal.—Dr. Jackson L. Sadler, Denver, assistant director of the maternal and child health division of the Colorado state board of health, has resigned to enter private practice in Fort Collins, it is reported.

Society News.—Dr. Clifford Lee Wilmoth discussed "Hepatic and Pleural-Hepatic Abscesses" before a meeting of the Medical Society of the City and County of Denver August 2. Dr. Charles Armstrong, U. S. Public Health Service, Washington, D. C., among others, addressed the society September 6 on the work of the service on epidemic encephalitis. The society was addressed October 4 by Drs. Harry Gauss on "Gastrointestinal Symptoms in Anorectal Disease" and Edward J. Meister, "Problems in Preoperative Irradiation of Carcinoma of the Heart."

FLORIDA

Regional Meeting.—The Florida East Coast Medical Association will meet in Rockledge October 28-29. Among the speakers will be:

Dr. Arthur J. Logie, Jacksonville, The Value and Significance of the Tuberculin Test.
Dr. Harold H. Fox, Miami, Oligurias with Blood Transfusions.
Dr. Fred Mathers, Orlando, Differential Diagnosis of Jaundice.
Dr. Evans B. Wood, Daytona Beach, Treatment of Coronary Occlusion.
Dr. Joseph S. Stewart, Miami, Psychological Aspect of the Diagnosis of Intestinal Obstruction.

Society News.—Drs. Efton J. Thomas, Miami Beach, and Edward W. Cullipher, Miami, addressed the Dade County Medical Society September 6 on "Jellyfish and Portuguese Man-of-War Stings" and "Common Foot Ailments" respectively.—At a meeting of the Leon-Gadsden-Liberty-Wakulla-Jefferson County Medical Society, Wakulla Springs, August 18, the speakers were Drs. Mark F. Boyd, Tallahassee, on malaria; Robert C. Pendergrass, Americus, Ga., the chronic cough, and Arthur J. Logie, Jacksonville, tuberculin tests.

GEORGIA

District Meetings.—The Fifth District Medical Society met in Atlanta October 6, with Dr. Howard M. Clute, Boston, as the guest speaker on "Diagnosis and Management of Acute Cholecystitis." Other speakers were Drs. Thomas C. Davison, Atlanta, on "Factors Influencing the Mortality of Ruptured Gastric and Duodenal Ulcers"; Grady N. Coker, Canton, "Some of Our Mistakes," and Maurice L. Blatt, Chicago, "Rabies."—The Fourth District Medical Society and the Georgia section of the Southeastern Surgical Congress held a

joint meeting at La Grange August 17. Among the speakers were Drs. Frederick J. Waas, Jacksonville, Fla., on hernia; Robert L. Sanders, Memphis, Tenn., diseases of the biliary system; Thomas P. Goodwyn, Atlanta, fracture of the neck of the femur, and Murdock S. Equen, Atlanta, acute mastoid.

ILLINOIS

Annual Branch Urologic Meeting.—The fifteenth annual meeting of the North Central Branch of the American Urological Association was held at the Pere Marquette Hotel, Peoria, September 30. The following were among the speakers:

- Dr. James T. Priestley, Rochester, Minn., Treatment of Bilateral Staghorn Renal Calculi.
- Dr. John K. Ormond, Detroit, Necrosis of Part of Kidney with Temporary Urinary Fistula Following Section of Aberrant Vessel.
- Drs. Henry O. Mertz and William E. Crump, Indianapolis, Leiomyosarcoma of the Spermatic Cord Complicated by Blood Dyscrasia: Report of Case.
- Dr. Sam W. Litzenger, Anderson, Duplication of Ureter with One Branch Ending Blindly: Case Report.
- Dr. John A. Fisher, Cincinnati, Congenital Unilateral Renal Agenesis: Brief Summary of the Literature with Reports of Two Interesting Cases.
- Dr. Seldon R. Hoover, Quincy, Ill., Prostatism in Women.
- Dr. Floyd C. Hendrickson, Canton, Ohio, Congenital Contracture of the Vesical Neck: A Report of Seven Cases.
- Dr. John H. Morrissey, New York, Treatment of Acute and Chronic Adnexal Suppuration.
- Dr. William N. Taylor, Columbus, Ohio, Mycotic Aneurysm.
- Drs. Dorris F. Rudnick and Alex B. Ragins, Chicago, Malacoplakia of Urinary Bladder.
- Drs. Henry B. Freiberg and Harry O. Lepsky, Cincinnati, Restoration of the Continuity of the Vas Deferens Eight Years After Bilateral Vasectomy.
- Dr. Gilbert J. Thomas, Minneapolis, Diagnosis and Treatment of Subacute and Chronic Lesions of Tuberculosis in the Genital Tract.
- Dr. Norris J. Heckel, Chicago, Benign Neoplasms of the Kidney with Report of a Papillary Cyst Adenoma.
- Dr. George H. Ewell, Madison, Wis., Traumatic Epididymo-orchitis.
- Dr. Harry A. Durkin, Peoria, Cardiac Care in Prostatic Surgery.
- Dr. Alf H. Gundersen, LaCrosse, Wis., Management of the Very Aged Prostatic with Report of Seventy-Five Cases of 75 Years Old with End Results.
- Dr. Clifford W. Losh, Des Moines, Iowa, Transurethral versus Suprapubic Prostatectomies.
- Dr. Victor J. LaRose, Bismarck, N. D., A Simple Apparatus for Controlling Traction on the Hemostatic Bag Catheter When Used After Transurethral Prostatic Resection.
- Dr. Charles H. McKenna, Chicago, Operative Technic of Hypospadias.
- Drs. Robert H. Herbst and James W. Merricks Jr., Chicago, Seminal Vesiculitis: A Study Carried Out by Retrograde Catheterization and Dilatation of the Ejaculatory Ducts with Visualization of the Seminal Vesicles.
- Dr. A. Jerome Sparks, Fort Wayne, Ind., Pericystitis.
- Dr. George C. Burr, Detroit, Uterovesical Fistula.
- Dr. William S. Ehrlich, Evansville, Ind., Demonstration of Some Useful Urologic Gadgets.

The North Central Branch derives its membership from Iowa, North and South Dakota, Minnesota, Wisconsin, Central Canada, Illinois, Indiana, Michigan and Ohio. Dr. Charles C. Higgins, Cleveland, was elected president; Dr. Bransford L. Adelsberger, Peoria, vice president, and Dr. William J. Baker, Chicago, secretary.

Chicago

Public Health Lectures for Nurses.—The Tuberculosis Institute of Chicago and Cook County will present a series of lectures on public health and social problems for graduate nurses, to be held during the next three months. Three groups of lectures are planned to be given at the University of Illinois College of Medicine, at the University Clinics, University of Chicago, and at Grant Hospital. The following physicians will be among the speakers:

- Drs. Hugo O. Deuss and William B. Tucker, Diagnosis of Tuberculosis.
- Drs. Max Biesenthal and Jerome R. Head, Treatment of Pulmonary Tuberculosis.
- Drs. George K. Fenn, Harold C. Lueth and George V. Le Roy, Heart Disease.
- Drs. John A. Wolfer and Max Cutler, Cancer.
- Dr. Paul A. Teschner, The Place of the Nurse in the Public Health Field.
- Drs. John A. Bigler and Arthur F. Abl, Infant Welfare and the Health of the Preschool Child.
- Dr. Arthur E. Mahle, The Place of Nutrition in a Public Health Program.

INDIANA

District Health Departments Confer.—The second annual conference of the district health department personnel was held at Indiana University, Bloomington, August 22-23. Speakers included Drs. John W. Ferree, Indianapolis, chief, bureau of local health administration, state board of health, who presided; Charles K. Kincaid, New Albany; Chester A. Hicks, Huntingburg; Lewis C. Robbins, Indianapolis, who presided at the second session, and Oliver W. Greer, Indianapolis.

New Agency to Supervise State Institutions.—The state welfare department has created a new division of medical care to supervise the work of the five state mental hospitals, two institutions for the feeble-minded, a village for epileptic patients, soldiers' home and sanatorium for tuberculosis. Dr. George C. Stevens, psychiatrist for the welfare department's division of correction, has been appointed director of the new division with Dr. Lillian G. Moulton as his assistant and Miss Nelle W. Massey as a nutritionist. According to newspaper accounts, points in the new program include: four annual inspections of each institution; investigation of all accidents and sudden, unnatural or violent deaths and recommendations for prevention of such accidents; the setting up and maintaining of suitable standards of care and psychiatric treatment; establishment of nutritious, yet economical dietary standards; passing on qualifications of personnel, and supervision of laboratories. Dr. Stevens was appointed to the division of correction last May.

MASSACHUSETTS

Dr. Strong Made Professor Emeritus.—Dr. Richard P. Strong, since 1913 professor of tropical medicine at Harvard University Medical School, has retired from that professorship with the title emeritus, according to the *New York Times*. Born in Virginia in 1872, Dr. Strong received his medical degree at Johns Hopkins University School of Medicine, Baltimore, in 1897. He served in the U. S. Army Medical Corps and as president of the board for investigation of tropical diseases in the Philippine Islands from 1899 until 1901. He established and directed the work of the Army Pathological Laboratory and directed the Government Biological Laboratory, Manila, from 1901 to 1913. He resigned from the army in 1902. He was professor of tropical medicine at the College of Medicine and Surgery, University of the Philippine Islands, from 1907 to 1913, then came to Harvard. He has been a member of the Massachusetts State Health Department since 1921 and has served as president of the following: Association of American Physicians, 1925-1926; Academy of Tropical Medicine, 1936; American Society of Tropical Medicine, 1914, and American Society of Parasitologists, 1914. Dr. Strong is a member of many scientific societies and has served as delegate to the meetings of numerous international organizations. Among other posts held during the World War he was director of the department of medical research of the American Red Cross. The Distinguished Service Medal is among the many honors bestowed on Dr. Strong.

MICHIGAN

Principal Causes of Death.—According to the state medical journal, in a total of 53,468 deaths in 1937 in Michigan, 37,477 were the combined toll of heart disease, cancer, apoplexy, pneumonia, coronary disease and angina, nephritis, accidents exclusive of automobile, automobile accidents, tuberculosis and diabetes. Heart disease caused 9,726 deaths, giving a mortality rate of 190.97 per hundred thousand population and showing the largest decrease in mortality from this cause in recent years; the 1936 rate was 197.04 when 10,010 deaths occurred. A slight decrease was noted for cancer. Apoplexy replaced pneumonia as the third major cause of death. Pneumonia accounted for 4,098 deaths; nephritis, 2,931 (the lowest in ten years); accidental deaths, excluding those caused by automobiles, 2,405; automobile deaths, 2,175 (an all time high); tuberculosis, 2,119; diabetes, 1,255. There were 91,566 births in 1937 with a rate of 17.98 per thousand population, the highest since 1931. The infant mortality rate was the lowest ever recorded with the exception of 1936. A new low maternal mortality rate was established in 1937. There were 326 deaths of mothers from causes connected with pregnancy and childbirth, giving a rate of 3.56 per thousand live births.

MINNESOTA

O'Leary, Unlicensed, Jailed.—L. Leo O'Leary, aged 23, pleaded guilty August 24 to a charge of practicing healing without a basic science certificate and received a suspended sentence of one year in the Clay County Jail from Judge Anton Thompson in the district court at Moorhead. A professional card in the *Barnesville Record Review*, July 7, read:

L. Leo O'Leary
Drugless Therapy
Electro-Hydro Therapy Treatments
Dietetics and Baths
Office at Broadway Hotel
Hours 1-6 and by appointment
Phone 72

He pleaded guilty after spending eight days in the Clay County Jail. O'Leary stated that he studied at the "National College of Drugless Physicians in Chicago," and also that he

started a three months correspondence course at the Swedish College of Massage in Chicago; that he was to pay about \$30 for the course but had paid only \$3 and received a half dozen lessons. He maintained office hours only in the afternoon and devoted his mornings to the sale of aluminum ware. In suspending the sentence, the judge told O'Leary that he was to refrain from practicing healing until he was licensed, to pay his personal obligations at Barnesville on or before March 1, 1939, and to pay the court costs within sixty days.

MISSISSIPPI

Personal.—Dr. George H. Wood, Batesville, has been made health officer of Panola County on a part time basis, succeeding the late Dr. Albert P. Alexander, Como.—Dr. Evan M. Gavin, Stafford Springs, was recently elected district commander of the seventh district of the American Legion; the district comprises the counties of Clarke, Jasper, Wayne, Jones, Covington, Smith and Simpson.

NEBRASKA

Annual Mid-West Clinical Meeting.—The annual Omaha Mid-West Clinical Assembly will be presented at the Hotel Paxton October 24-28 with the following speakers:

- Dr. Robert T. Frank, New York, Treatment of Rectocele, Cystocele and Prolapse of the Uterus; Treatment of Functional Diseases.
- Dr. Heyworth N. Sanford, Chicago, Hemorrhagic Diseases of Infancy and Childhood; Cerebral Hemorrhage of the New-Born.
- Dr. Foster Kennedy, New York, The Organic Background of Mind; Epilepsy; Insanity as a Defense in Crime.
- Dr. Henry L. Bockus, Philadelphia, Practical Application of Recent Advances in Our Knowledge of Liver Function; Diagnosis and Treatment of Chronic Gastritis.
- Dr. Cameron Haight, Ann Arbor, Mich., Practical Considerations Relating to Acute and Chronic Empyema; Diagnosis and Management of Carcinoma of the Lung.
- Dr. Oliver H. Perry Pepper, Philadelphia, Principles of Diagnosis and Treatment of Disease in the Elderly; Recognition and Treatment of Anemia Due to Increased Blood Destruction.
- Dr. Gordon B. New, Rochester, Minn., Diagnosis of Laryngeal Lesions; Deformities of the Face Corrected by Plastic Surgery.
- Dr. Edward L. Jenkinson, Chicago, Value of Repeated Cholecystography and the Effect of Medical Management on the Visualization of the Gallbladder; Roentgen Examination of the Small Bowel.
- Dr. Alfred R. Shands Jr., Wilmington, Del., Osteomyelitis in Children; Post-Poliomyelitis Problems.
- Dr. Oliver S. Ormsby, Chicago, Precancerous Dermatoses; Contact Dermatitis.
- Dr. Louis J. Hirschman, Detroit, The Rationale of Internal Hemorrhoidectomy; The Two-Stage Operation for Anal Fistula.
- Dr. Ralph M. Waters, Madison, Wis., Development of Anesthesiology.
- Dr. John S. Lundy, Rochester, Minn., Indications for Rectal, Intravenous, Spinal and Regional Anesthesia.
- Dr. Kenneth C. McCarthy, Toledo, Ohio, Anesthesia for Bad Risk Patients.

A symposium on anesthesia will be presented by Drs. Archibald R. McIntyre, Omaha, and Robert Maxwell Grier, Evanston, Ill. Clinics will be held every afternoon.

NEW MEXICO

First Evidence of Plague Infection.—The U. S. Public Health Service reported August 20 that plague infection had been proved in prairie dogs, in pools of fleas from prairie dogs and field mice in Catron County. This is believed to be the first evidence of the existence of plague in the state.

NEW YORK

District Meeting.—The Third District Branch of the Medical Society of the State of New York held its annual meeting at Cobleskill September 20 with the following program:

- Dr. Frederick A. D. Alexander, Albany, Modern Anesthesia.
- Dr. Morris A. Goldberger, New York, Modern Trends in Obstetric Practice.
- Dr. Thomas Wood Clarke, Utica, Allergic Manifestations in the Central Nervous System.
- Dr. Donald Guthrie, Sayre, Pa., Diagnosis and Treatment of Hyperthyroidism.
- Dr. Louis K. Diamond, Boston, Anemia in Children.
- Dr. Charles G. Heyd, New York, Diagnostic Interpretation of Jaundice.

Examination of Food Handlers Believed Ineffective.—The New York State Association of Public Health Laboratories recently adopted a resolution declaring that routine laboratory examinations of food handlers, milk handlers and domestic servants are ineffective as a protection of the public health and approving repeal of any existent legislation or mandatory regulation requiring such tests as routine. The resolution pointed out that many public health authorities have seriously questioned the value of such examinations and that when results are negative a false sense of security may be engendered. It also suggested that the performance of the tests requires financial outlay with no commensurate return to public health.

New York City

Manson-Bahr Lectures on Dysentery.—Dr. Philip E. C. Manson-Bahr, School of Tropical Medicine, London, conducted a clinic on bacillary dysentery September 30 for students and guests of the Long Island College of Medicine. A case of proved *Shigella dysenteriae* infection in a seaman from Calcutta was presented from the tropical disease service of the Long Island College Hospital. After discussion of the case Dr. Manson-Bahr spoke on dysentery, illustrating his talk with epidiascope projections of his collection of original drawings.

Society News.—Drs. Foster Kennedy and Elizabeth I. Adamson addressed the Medical Society of the County of Queens, September 27, on "The Organic Background of Mind" and "Mild Depressions Cared for by the Family Doctor" respectively. The society will present a series of lectures on skin disease November 14-17, with the following lecturers: Drs. Ida J. Mintzer, Jamaica, on "Common Skin Conditions"; Charles S. Miller, "New Growths of the Skin"; Joel Schweig, "Parasitic Diseases of the Skin" and Rudolph Boenke, "Therapeutics of Common Skin Diseases."—Dr. Arthur W. Grace gave a Friday afternoon lecture before the Medical Society of the County of Kings, Brooklyn, October 7, on "Lymphogranuloma Venereum"; Dr. William S. Collens spoke October 14 on "Diagnostic and Therapeutic Aspects of Peripheral Diseases."—A symposium on "The Future of American Medicine" will be held in the grand ballroom of the Hotel Center October 21 under the auspices of the Interne Council of America. The two principal speakers will be Drs. John P. Peters, professor of medicine, Yale University School of Medicine, New Haven, Conn., and Philip I. Nash, president-elect of the Medical Society of the County of Kings.

NORTH CAROLINA

Professor Appointed.—Dr. John W. Roy Norton, assistant director of preventive medicine, state board of health, Raleigh, has been appointed professor of public health administration in the division of public health, University of North Carolina School of Medicine, Chapel Hill. Dr. Norton graduated from Vanderbilt University School of Medicine, Nashville, Tenn., in 1928 and was for several years health officer of Rocky Mount before joining the state board of health.

OHIO

Personal.—Dr. Rollin D. Worden, Ravenna, resigned September 1 as health commissioner of Portage County. Dr. Percy L. Harris, Columbus, now a member of the staff of the state health department, succeeds Dr. Worden.—Dr. Carl J. Wiggers, professor of physiology, Western Reserve University School of Medicine, Cleveland, sailed September 9 for South America to give a series of lectures in Chile and Argentina.

Society News.—Dr. Edward William Alton Ochsnor, New Orleans, addressed the Academy of Medicine of Cleveland September 16 on "Management of Peripheral Vascular Disease."—Mr. R. H. Nesbitt, Akron lawyer, addressed the Summit County Medical Society, Akron, September 6, on "The Doctor and the Law."—Dr. Perrin H. Long, Baltimore, addressed the Mahoning County Medical Society, Youngstown, September 20, on sulfanilamide.

District Meeting.—The Fifth District Medical Society will meet at the Medical Library Auditorium in Cleveland October 21 to hear the following program:

- Dr. Arthur D. Nichol, Clinical Observations on the Hyperactive Carotid Sinus.
- Dr. Abraham Strauss, The Management of Undescended Testes with Demonstration of Cases.
- Dr. Edmund E. Beard, Endocrine Aspects of Pituitary Tumors.
- Dr. Gerald S. Shibley, Treatment of Pneumonia.
- Dr. John A. Toomey, Treatment of the Meningitides.
- Dr. Curtis F. Garvin, The Dangers of Sulfanilamide Therapy.
- Dr. Raymond C. McKay, Early Diagnosis and Treatment of Pulmonary Tuberculosis.
- Dr. Edward E. Woldman, A Simple Test for Determining the Presence of Gastrointestinal Lesions.
- Dr. Thomas E. Jones, Treatment of Carcinoma of the Rectum.

The general meeting in the evening will be under the auspices of the Academy of Medicine of Cleveland with Dr. Clifford J. Barborka, Chicago, speaking on "The Management of Nutritional Diseases." Drs. Hubert C. King and Barney J. Hein, Toledo, presidents respectively of the academy and the state medical association, will also speak.

OKLAHOMA

New Health Officers.—Dr. Ferdinand R. Hassler Jr., formerly of Oklahoma City, has been appointed director of a new city and county health unit in Muskogee and Muskogee County.—Dr. James O. Hood, Norman, has been appointed health officer of Cleveland County to succeed Dr. Guy H. Williams.

OREGON

Hospital News.—The Dr. Robert C. Coffey Clinic and Hospital, Portland, will henceforth be known as the Coffey Memorial Hospital in memory of Dr. Coffey, who was killed in an airplane accident Nov. 9, 1933.—A new \$250,000 hospital with forty-three beds has been completed at La Grande; it will be known as St. Joseph's Hospital.

New Buildings for the University.—A laboratory building and a library with an auditorium are to be built immediately at the University of Oregon Medical School, Portland, it was announced September 10, when a PWA grant of \$163,000 was approved. This grant augments a gift of \$100,000 from Dr. John E. Weeks, retired physician of Portland, and a grant of \$100,000 from the Rockefeller Foundation. Plans call for a library building of reinforced concrete, containing an auditorium, track rooms, reading rooms, study rooms and a lobby. It will be connected by a passage with the three story laboratory building, which will be an extension of the west wing of the medical school. The library contains about 30,000 volumes.

PENNSYLVANIA

Annual Seminar.—The ninth annual postgraduate seminar will be presented at the Easton Hospital, Easton, October 26. The speakers will be:

- Dr. John de J. Pemberton, Rochester, Minn., Surgery of Diseases Associated with Splenomegaly.
- Dr. William Halsey Barker, Baltimore, Clinical Use of Sulfanilamide.
- Dr. Frank C. Hamm, Brooklyn, Kidney Conditions in Children.
- Dr. Harrison F. Flippin, Philadelphia, Undulant Fever.
- Dr. Thomas T. Mackie, New York, Pathological Histology and Amebic Colitis.
- Dr. Lewis K. Ferguson, Philadelphia, Newer Methods in the Management of the Surgical Ambulatory Patient.

Philadelphia

Hospital Lectures.—Mount Sinai Hospital opened its seventh annual series of health talks for the public September 21 with a talk by Dr. Samuel E. Rynes entitled "How Many People Are Allergic?" Dr. Sigmund S. Greenbaum will speak October 19 on "Cosmetics and Skin Health" and Dr. Theodore H. Mendell, November 16, on "High Blood Pressure—The Threat to Long Life."

Society News.—Drs. Rudolf L. Roddy, James S. Forrester and Harold Landow addressed the Obstetrical Society of Philadelphia October 6 on "Management of an Institutional Outbreak of Infectious Diarrhea of the Newborn" and Dr. Richard Manges Smith, "X-Ray Localization of the Placenta by Soft Tissue Technic and Without the Use of Opaque Media."—At a meeting of the Philadelphia Academy of Surgery October 10 the speakers were Drs. Isidor S. Ravdin, Harry E. Knox and Calvin M. Smyth Jr., on "The Problems of Acute Appendicitis with Peritonitis" and Ernest G. Williamson and Lynn M. Rankin, "Management of Appendicitis Complicated by Peritonitis with Special Reference to Postural Drainage."

TENNESSEE

Personal.—Dr. David M. Cowgill, Madisonville, health officer of Monroe County, has been appointed director of the Giles County health unit. He succeeds Dr. J. W. Erwin, Pulaski, who has been appointed in Washington County.

University News.—Miss Frances Helen Zeigler, R.N., dean of the school of nursing and director of nursing service at the Medical College of Virginia, Richmond, has been appointed dean of the school of nursing at Vanderbilt University, Nashville.

Society News.—Drs. Conley H. Sanford and Neuton S. Stern, Memphis, addressed the Madison County Medical Society, Jackson, September 6, on "Medical Management of Gallbladder Disease" and "Coronary Sclerosis, Angina Pectoris and Coronary Occlusion" respectively.—Dr. Frank H. Booher, Lynchburg, addressed the Bedford County Medical Society July 21 in Shelbyville on meningitis.

TEXAS

Dates Set for Clinical Conference.—The Dallas Southern Clinical Society announces that the eleventh annual spring conference will be held March 13-16 at the Hotel Adolphus. The guest speakers will be Drs. Fuller Albright, Richard B. Cattell, Charles F. McKhann, Boston; Sanford R. Gifford, Robert H. Herbst and Harry E. Mock, Chicago; Louis J. Karmosh, Cleveland; Dean M. Lierle, Iowa City; William S. Middleton, Madison, Wis.; Alfred C. Reed, San Francisco; Wendell G. Scott, St. Louis, and Richard W. Telinde, Baltimore. Dr. George A. Schenewerk is secretary of the society.

Post Graduate Assembly in Houston.—The seventh Post Graduate Medical Assembly of South Texas will be held at the Rice Hotel, Houston, November 1-3, with the following guest speakers:

- Dr. Francis Heed Adler, professor of ophthalmology, University of Pennsylvania School of Medicine, Philadelphia.
- Dr. Fremont A. Chandler, assistant professor of orthopedic surgery, Northwestern University Medical School, Chicago.
- Dr. Carey Culbertson, clinical professor of obstetrics and gynecology, Rush Medical College, Chicago.
- Dr. Louis J. Hirschman, professor of proctology, Wayne University College of Medicine, Detroit.
- Dr. Robert Louis Levy, professor of clinical medicine, College of Physicians and Surgeons, Columbia University, New York.
- Dr. Thomas T. Mackie, New York.
- Dr. Harvey B. Matthews, clinical professor of obstetrics and gynecology, Long Island College of Medicine, Brooklyn.
- Dr. Henry G. Poncher, associate professor of pediatrics, University of Illinois College of Medicine, Chicago.
- Dr. Mont R. Reid, professor of surgery, University of Cincinnati College of Medicine, Cincinnati.
- Dr. Lyman G. Richards, associate professor of otolaryngology, Tufts College Medical School, Boston.
- Dr. John J. Shea, Memphis, Tenn.
- Dr. Edward H. Skinner, Kansas City, Mo.
- Dr. Gilbert J. Thomas, clinical associate professor of urology, University of Minnesota Medical School, Minneapolis.
- Dr. Derrick T. Vail Jr., professor of ophthalmology, University of Cincinnati College of Medicine, Cincinnati.
- Dr. Carroll S. Wright, professor of dermatology and syphilology, Temple University School of Medicine, Philadelphia.

Meetings will be in general sessions, except for one section on diseases of the eye, ear, nose and throat. An innovation this year will be question and answer periods. There will be scientific and technical exhibits and motion pictures each day.

VIRGINIA

Society News.—At a meeting of the Southside Virginia Medical Association, Burkeville, September 13, the speakers included Drs. Thomas F. Wheeldon, Richmond, on "The Use of Metal Tubes in Osteomyelitis"; John A. Proffitt, Burkeville, "Pleural Effusions" and Wellford C. Reed, Richmond, "Significance and Management of Ankle Edema."—Richmond physicians addressed the quarterly meeting of the Mid-Tidewater Medical Society in Gloucester July 27, as follows: Drs. John L. Tabb Jr., on "X-Ray Treatment of Sinusitis"; William L. Peple, "Clinical Classification and Treatment of Cancer of the Cervix"; James H. Smith, "Abnormalities of the Thyroid" and Donald M. Faulkner, "Treatment of Fracture of the Hip with the Nail."

Testimonial to Dr. McGuire.—The Richmond Academy of Medicine gave an informal testimonial dinner in honor of Dr. Stuart McGuire September 27 at the Commonwealth Club, Richmond, in appreciation of his interest in and devotion to the academy. Dr. Austin I. Dodson, president of the academy, introduced Dr. John Shelton Horsley, chairman of the dinner committee, who presented the toastmaster, Frederic W. Boatwright, LL.D., president of the University of Richmond. Dr. John M. T. Finney, emeritus professor of surgery, Johns Hopkins University School of Medicine, Baltimore, was the chief speaker. A portrait of Dr. McGuire was presented to the academy on behalf of a group of donors by Dr. Roshier W. Miller and Dr. McGuire received a portfolio of letters. Dr. McGuire, who is 71 years old, graduated from the University of Virginia in 1891. He is emeritus professor of surgery at the Medical College of Virginia, of which he also served as president from 1914 to 1925. He was president of the Medical Society of Virginia in 1908.

WASHINGTON

Hospital News.—A new \$126,000 dispensary was placed in service at the Puget Sound Navy Yard, Bremerton, in August.

—St. Martin's Hospital, a new \$50,000 institution at Tonasket, Wash., was dedicated August 25 by the Bishop of Spokane.

Society News.—Dr. Walter L. Palmer, Chicago, addressed the Spokane County Medical Society, Spokane, September 8, on "Treatment of Benign Conditions of the Gastrointestinal Tract."—Dr. Donald A. Murray, Seattle, addressed the King County Medical Society, Seattle, September 19, on "Fractured Hips Treated by Smith-Petersen Nails."

WISCONSIN

Personal.—Dr. Mina B. Glasier, Bloomington, recently resigned as a member of the state board of health after fourteen years of service. She served as president of the board in 1935 and as vice president in 1937.—Dr. Myrie G. Peterman, Milwaukee, has resigned as professor of pediatrics at the Marquette University School of Medicine, effective September 1. He was appointed in 1928.

PUERTO RICO

Hospital News.—It is reported that Dr. Thomas D. Slagle, Coamo, has been appointed superintendent of St. Luke's Memorial Hospital, Ponce, a sixty-five bed hospital supported by the Episcopal Church. Dr. Slagle, a native of North Carolina, graduated from Cornell University Medical School, New York, in 1932.

GENERAL

Society Seeks Information on Eye Hazards.—The National Society for the Prevention of Blindness requests information on industrial or occupational eye hazards for a new edition of "Eye Hazards in Industrial Occupation." The request specifies: (1) information concerning new industrial or occupational eye hazards—both accident and disease hazards; (2) recent and significant statistics concerning any occupational hazards to sight, showing frequency, severity, causes, nature of injury, degree of impairment, cost, etc.; (3) photographs showing either hazards to sight or protection against such hazards, and (4) information concerning successful methods of eliminating, counteracting or alleviating the disease and accident hazards to eyes. The society's headquarters are at 50 West Fiftieth Street, New York.

Association of American Medical Colleges.—The forty-ninth annual meeting of the Association of American Medical Colleges will be held in Syracuse, N. Y., October 24-26 under the presidency of Dr. Alan M. Chesney, Baltimore. The speakers will include:

Dr. Thomas Parran, surgeon general, U. S. Public Health Service, Washington, D. C., Future of the Public Health Movement.
Dr. Reginald Fitz, Boston, When and How Shall Interns Be Appointed?
Dr. Edward C. Hughes, Syracuse, Use of the Home Delivery Service in Syracuse in the Teaching of Obstetrics.
Dr. Joseph Earle Moore, Baltimore, Teaching of Syphilis.

There will also be a symposium on "The Place of Preventive Medicine in the Medical Curriculum," presented by Drs. John G. Fitzgerald, Toronto; Waller S. Leathers, Nashville, Tenn.; Frederick F. Russell, Boston, and Harry S. Mustard, New York.

American Public Health Association.—The sixty-seventh annual meeting of the American Public Health Association will be held in Kansas City October 25-28. Among numerous speakers who will address section meetings are:

Dr. George C. Ruhland, Washington, D. C., The Objectives of Health Departments.
Dr. Philip C. Jeans, Iowa City, Nutritional Requirements During Growth.
Drs. Thomas B. Turner, Baltimore; Abraham L. Gelperin, Cincinnati, and James R. Enright, Honolulu, Hawaii, Results of Contact Investigation in Syphilis in an Urban Community.
Dr. George McL. Lawson, Charlottesville, Va., Immunity Studies in Pertussis.
Dr. Thomas F. Sellers, Atlanta, Ga., Laboratory Diagnosis of Rabies.
Reuben L. Kahn, Sc.D., Ann Arbor, Mich., Fifteen Years of the Standard Kahn Test.
Franklin C. Bing, Ph.D., secretary, Council on Foods, American Medical Association, Chicago, Advances in Our Knowledge of Nutrition.
Harry B. Meller, managing director, Air Hygiene Foundation of America, Pittsburgh, Practical Procedures and Limitations in Present-Day Smoke Abatement.
Dr. Paul A. Teschner, assistant director, Bureau of Health Education, Chicago, The Doctor Looks at the Voluntary Health Agency.

Dr. Arthur T. McCormack, Louisville, Ky., president of the association, will make his official address at a general session and Dr. Thomas Parran, surgeon general, U. S. Public Health Service, Washington, D. C., will speak at another. Among symposiums will be those on industrial hygiene administration, venereal disease control, outposts of research and new facts for the health educator. A number of other organizations will hold meetings during the week, including the American School Health Association, the Association of Women in Public Health, the American Association of State Registration Executives and International Society of Medical Health Officers.

Research Council on Problems of Alcohol.—The American Association for the Advancement of Science has announced the appointment of the Research Council on Problems of Alcohol to make a scientific investigation of the problems related to the control of alcoholic beverages. Dr. Karl M. Bowman, director of the division of psychiatry, Bellevue Hospital, and professor of psychiatry, New York University College of Medicine, is chairman of an executive committee of fifteen members of which ten are required to be scientists. Hans T. Clarke, D.Sc., professor of biochemistry, Columbia University, is chairman of the scientific committee and Willard E. Givens,

executive secretary of the National Education Association, has been elected chairman of the educational committee. Mr. Harry H. Moore, formerly director of the Committee on Costs of Medical Care, has been chosen director of the council's activities with headquarters in New York. The primary objective of the council is to develop the sociologic and biologic facts paramount in the control of alcoholic beverages and secondly to make them available to the public. In outlining its program of research, the council will take into account other adequate studies in the field which have already been conducted, which may be contemplated and which may be under way, and it will assign each of its own studies, so far as practicable, to other research agencies, such as universities, hospitals and professional organizations. Finally, it will constantly seek to integrate the results of all studies for the purpose of resolving contradictions, of filling gaps in existing knowledge and of making available a reasonably complete and well organized body of factual data.

Changes in Status of Licensure.—The board of medical examiners of Maryland recently reported the following action:

Dr. Paul F. Wiest, Charlestown, W. Va., license suspended July 7 on his conviction of violation of the Harrison Narcotic Act.

The Minnesota State Board of Medical Examiners reports the following action:

Dr. Harold Rees, Ogilvie, Minn., license revoked May 13 for "habitual indulgence in the use of narcotics."

The Virginia state board of medical examiners reports the following:

Dr. Calvin Howard Cain, Orange, license revoked June 22 for violation of the federal narcotic laws.

Dr. Robert Scott Fitzgerald, Richmond, license revoked June 22 on account of conviction of performing an illegal operation.

The Arizona State Board of Medical Examiners announces the following:

Dr. Nathaniel D. Hightower, Phoenix, license restored July 6; placed on probation for five years and as long as a resident of Arizona to be without narcotic permit.

Dr. Richard McClellan Francis, Flagstaff, license restored July 6; placed on probation for five years and as long as a resident of Arizona to be without narcotic permit.

The Wisconsin State Board of Medical Examiners reports the following action:

Dr. Raymond James Henderson, Tomahawk, license revoked July 1 for having performed illegal operations.

CANADA

Personal.—Dr. John W. McIntosh, medical officer of health of Vancouver, B. C., retired from that position September 30.

—Dr. Pio H. Laporte, Edmundston, has been appointed minister of health and labor in the government of New Brunswick.—Dr. Randolph J. Gibbons, formerly assistant to the director of the Connaught Laboratories, University of British Columbia, Vancouver, has been appointed chief bacteriologist to the laboratory of hygiene, department of pensions and national health.

FOREIGN

Institute of Hematology in Paris.—A center for blood transfusion was opened at Saint Antoine Hospital in Paris in June, gift of Madame Deutsch de la Meurthe, a Paris philanthropist. The institute of hematology consists of four divisions: the central services where donors are registered and where requests are received; a library on hematology; a laboratory for work in connection with current needs, and a laboratory for research in hematology, including a study of preserved blood.

Personal.—Sir Arthur Newsholme, Worthing, England, received the Jenner Medal of the Royal Society of Medicine "for distinguished work in epidemiologic research or for pre-eminence in the prevention and control of epidemic disease," according to *Science*.—Mr. Wilfred B. L. Trotter, director of the surgical unit at the University College Hospital, London, has received the gold medal of the Royal Society of Medicine, awarded triennially to a "scientist, man or woman, who has made valuable contributions to the science and art of medicine."—Dr. James L. Maxwell, Shanghai, China, former editor of the *Chinese Medical Journal*, has been made a Commander of the Order of the British Empire.—At the recent meeting of the British Medical Association the Sir Charles Hastings clinical prize was presented to Dr. John W. McFeeters, according to *Science*.—The Dr. Jessie MacGregor prize in medical science of the Royal College of Physicians of Edinburgh has been awarded to Dr. Susanne J. Paterson for her work on the therapeutic uses of progesterone.

Foreign Letters

LONDON

(From Our Regular Correspondent)

Sept. 24, 1938.

The Control of Smallpox

The minister of health has issued a memorandum on smallpox in which he draws the attention of local authorities to the possibility of preventing or limiting the spread of the disease by prompt and vigorous action. A recent survey of the world distribution of smallpox shows that the strains in different countries are of different degrees of virulence and breed true over a long series of years. In India, the Far East and Northern Africa, the prevailing strain is virulent, producing variola major, while in England, Canada, the United States, the West Indies, Brazil and South Africa, the strain is nonvirulent, producing variola minor, known also as *alastrim* or *amaas*. In some of these countries the importation of the virulent strain showed the great difference between the two forms of the disease. In England the years 1920 and 1921 marked the disappearance of variola major as a serious administrative problem and the rise of variola minor to epidemic proportions. In 1917 the number of notifications of smallpox in England and Wales fell to seven; it then rose until 1927, when it reached 14,767, after which it steadily declined. In 1920 nearly all the cases were of variola minor, although outbreaks of variola major arose from the importation from abroad of a case of this form. In 1936 all the reported cases were of variola major, which in some instances was certainly, and in others probably, imported from abroad. Prompt action by the local authorities rapidly brought the outbreaks under control. Variola major has proved easier to check than variola minor, because people are alarmed by the more virulent condition and are willing to submit to all the methods of control. The international conditions in force, the vigilance of the port health authorities and the cooperation of the public have much reduced the risk of variola major reaching epidemic proportions in this country.

Variola minor is more difficult to control because its mildness leads to an attack's being unrecognized or recognized too late for exposed persons to receive the protection of vaccination. Also when persons begin to notice the mildness of the disease and that it does not kill or disfigure they are less disposed to submit to vaccination. Finally, the absence of alarm, or its subsidence, increases the difficulty of making inquiries and tracing persons who have been exposed to infection. The prominence given to cases of vaccinal encephalitis, rare though these are, also has discouraged vaccination, even after exposure to infection. Hence in spite of great efforts and much expenditure, variola minor has smoldered in some parts of the country.

The following procedure has been laid down by the minister of health: 1. The health officer should visit the patient with the physician in attendance. If smallpox is found the patient should at once be removed to the smallpox hospital. 2. The health officer should forthwith report to the ministry. 3. Vaccination or revaccination should be offered to exposed persons, and it should be kept in mind that the incubation period is to be taken as twelve days, or fourteen days to the characteristic focal rash; that if this period is divided into three intervals of seven, three and four days, successful vaccination in the first will prevent the attack, in the second will modify the eruption and in the third will have no influence; that the pertinent date is, however, not when vaccination is performed but when the reaction begins; that if the reaction, which should be manifest on the third or fourth day, is delayed by any cause, the rise of immunity is deferred, and that prevention can therefore be secured only by vaccination within a day or two of exposure. 4. Exposed persons should be kept under observation for sixteen

days after the last exposure to infection, but it is seldom necessary or desirable to isolate them in their homes. 5. The health officer should at once inform the public vaccinators so as to secure prompt vaccination of persons willing to be protected. 6. The infected house, its contents and the clothing of all who have been in close contact with the patient should be disinfected. 7. All persons with doubtful attacks should be seen at once by the health officer, and to this end physicians in the district should be notified of the presence of smallpox. 8. The health officer should notify the health officers of adjoining areas. 9. To ascertain the source of infection, careful inquiry should be made concerning the movements of the patient in the three weeks preceding the attack, particularly on the twelfth and fourteenth days prior to the onset.

Revision of Medical Standards for the Navy

The need for obtaining more men for the navy and army has led to some revision of the high standard of physical fitness which has been maintained. The standard for the navy is so high that only 25 per cent of the applicants are accepted. Only some slight relaxation has now been introduced. Except in certain branches, such as the seamen and signal branches, the men may now wear glasses to enable them to carry out their duties if they are medically fit in other respects, each case being considered on its merits by the commanding officer. For men who require spectacles when antigas respirators are worn, the side pieces are to be flattened so as to prevent leakage and the fit of all such frames is to be tested in a gas chamber. As a temporary expedient the dental standard of men who are fit in other respects and who are willing to receive treatment to render them fit for general service has been modified. Artificers and artisans for direct entry are not to be rejected for dental defects which can be remedied by treatment, which will include the free supply of dentures. Candidates for the rating of ordinary seamen who are wearing a satisfactory denture may be accepted, provided any natural teeth present are sound or readily conservable. In other ratings men who are below the normal dental standard only by loss of one pair of opposing molars may be accepted.

Casualties of Air Raids

The ministry of health has made rapid progress in organizing hospital accommodations to meet any emergency that may arise from air raids. In August the hospital authorities were told that in the event of a raid they would be expected to empty as many beds as possible by sending home patients fit to go. It is estimated that most hospitals could clear from 30 to 50 per cent of their beds in this way. The great majority of patients going home would be sitting or walking patients, and hospitals have been asked to arrange for their transport by voluntary organizations. Once at home, the patient would come under the general arrangements for evacuation of his district. Simultaneously certain hospitals, for the most part the larger general ones in the more congested areas, would "decant" patients fit to be moved, though not yet to go home, to other institutions capable of continuing their treatment but less useful for receiving air raid casualties. In the London area thirty-four hospitals have already been designated for decanting, and plans have been prepared for removing between 3,000 and 4,000 patients by ambulance trains to towns 50 miles or more from London. They would be conveyed to the railway stations by motor coaches converted to carry stretchers. Conferences have been held with all the representatives of the voluntary and municipal hospitals and with the health officers in the counties around London. Arrangements have been made in the towns which will receive patients from London for meeting the ambulance trains and conveying the patients to the hospital. The London County Council is providing surgical equipment at some of its larger hospitals not at present used for surgical cases, so that they can deal with casualties. So far the plans have been concerned principally with the utilization of existing accom-

modations, but the ministry of health has also taken steps for the acquisition of additional equipment, which will be distributed to different centers. Information has also been collected about the stocks of bedsteads, bedding and other equipment held by the trade in the various towns.

Sulphanilamide Added to the Poisons List

Sulphanilamide has been added to the official poisons list as a substance which may be supplied by pharmacists only on the written prescription of a physician, dentist or veterinary surgeon and is thus brought under the restrictions that apply to amidopyrine, barbituric acid, dinitroresol and sulphonal. Hitherto its sale has been unrestricted. This regulation will apply not only to sulphanilamide but to related substances sold under the names of Colsulanyde, P. A. B. S., Prontosil Album, Prontosil Rubrum, Prontosil Soluble, Streptocide, Sulphonamide Emulsion, Proseptasine, Roidlone, Rubiazol and Uliron. The calamity by which seventy-three persons lost their lives in the United States by taking a preparation known as elixir of sulfanilamide has no doubt influenced the Poisons Board in its decision.

Prison for Driver Suffering from Paralysis

Almost the only condition of a driver of an automobile which gives rise to prosecution is alcoholism. A driver, aged 38, who killed a cyclist has been found guilty of manslaughter, sentenced to twelve months' imprisonment and disqualified for life from holding a driving license. When he was arrested his symptoms suggested alcoholism, but he was found to be suffering from "creeping paralysis." When asked how he applied his brake he said that, owing to his condition, he used his hand to assist his leg. He had suffered from trench fever in the war, for which he was awarded a pension, and the police gave him an excellent character.

Code of Ethics for Pharmacists

At the conference of the British Pharmaceutical Society in Edinburgh a code of ethics for pharmacists was discussed and approved. Among other provisions of the code, it is laid down that if a dispenser detects an error in a physician's prescription it is his duty to protect both the customer and the reputation of the physician by conferring confidentially with the latter. The code forbids pharmacists to discuss with patients the composition of medicine and enjoins on them that every precaution be taken to safeguard the public from poisons and all habit-forming drugs and to use no exaggerated claims for medicines.

PARIS

(From Our Regular Correspondent)

Sept. 17, 1938.

Incidence of Pulmonary Tuberculosis in Miners

At the July 5 meeting of the Académie de médecine of Paris, the results of a study of the incidence of pulmonary tuberculosis in miners from 1923 to 1937 in the Saint-Etienne region were reported by Drs. Crozier and Martin. They said that there were very few recent statistics available. In most articles the statement is made that the incidence is about the same for miners as for other persons. The authors were also of this opinion until they had occasion to observe a large number of cases of pulmonary tuberculosis in a hospital owned by a large coal mining company. At times nearly half of the patients had pulmonary tuberculosis, and the average was one third of the hospital capacity. Between 1923 and 1937, 23.6 per cent of the hospital deaths were due to pulmonary tuberculosis, whereas the percentage for men of the same age who were not coal miners was only 16.5. The mortality rate for all males of the Saint-Etienne region who were not engaged in coal mining during 1936, the only year for which statistics are available, was 2.4 per thousand, as compared to 3.4 per thousand for coal miners. These statistics are surprising because, as a rule, coal miners

are in the best possible condition, a complete physical examination being obligatory before they are employed. The authors attempted to explain the relatively high incidence of pulmonary tuberculosis in coal miners by the fact that, first, most of the miners come from the country and fail to become adapted to city life; second, that alcoholism and poor living conditions play an important part, and, finally, that the dust-laden atmosphere and the necessity of working in a narrow space are important predisposing causes. As prophylactic measures, the authors had suggested better housing conditions, more adequate ventilation of mines, and the calling of attention to the dangers of alcoholism. Since these measures have been employed, an encouraging decrease in the mortality rate for pulmonary tuberculosis has been noted.

The Use of Virus Vaccine Against Plague

The use of living plague bacilli (*Pasteurella pestis*), as a prophylactic measure has been given a three year trial in the large French colony of Madagascar. The results of this vaccination were submitted in a paper read by Drs. G. Girard and J. Robic at the July 5 meeting of the Académie de médecine of Paris. In 1921 there were only 187 cases of plague, but in 1935 the number rose to 3,493. As a result of intensive use of the virus vaccine, the number of cases dropped to 2,006 in 1936 and to 918 in 1937. This recession is still more marked so far (first five months) in 1938. The number of vaccinated and revaccinated persons has passed 2,000,000. The results have been infinitely better since living vaccines have been used. The mortality rate has been lowered by 80 per cent. As long as it is impossible to eliminate the animal reservoir of the bacillus, it will be necessary to continue to vaccinate every native.

Persistence of Virulence of Cholera Vibrio

It is generally admitted that the resistance of the cholera vibrio to heat and desiccation is not great. The slight resistance of the cholera spirillum, especially its sensitiveness to drying, explains the rapid and complete disappearance of cholera in once infected localities and also the fact that the disease is rarely transmitted by aerial infection. In a paper read at the July 5 meeting of the Académie de médecine of Paris by Jean Laigret and Mme. P. Auburtin, the results are reported of a recent study as to whether the cholera vibrio is as sensitive to heat and desiccation as was hitherto believed. Laigret, in collaboration with Roger Durand, had previously shown that under certain conditions the bacillus of plague can be dried without destroying its vitality. Laigret and Auburtin have since found that the cholera vibrio also can be viable after desiccation. They utilized four strains which are used in Indo-China and China in the preparation of an anticholera vaccine. The desiccation technic was that employed by the Pasteur Institute of Tunis in the preparation of the living virus vaccines against yellow fever and typhus. When the desiccated cholera vibrios were inoculated on various mediums at various intervals they showed an active growth as late as thirty-two days after desiccation. This discovery is of great importance from the standpoint of epidemiology. In all countries where cholera is endemic and there are dry and wet seasons, it has been noticed that the earliest attacks always appear after the first rain. Hitherto some native or foreign carrier has been blamed, but in view of this research by Laigret and Auburtin, the question arises whether this is true in all cases, although the natural methods of desiccation in all probability can act so as to keep the cholera vibrio alive longer than is possible so far in laboratory work. The virus of typhus, as has been shown by Nicolle for dried excreta and by Georges Blanc for lice, can remain virulent for months. The desiccation of the cholera vibrio under natural conditions and its recrudescence when in contact with water may serve to explain the annual recurrence of epidemics in countries where there are dry and wet seasons.

BERLIN

(From Our Regular Correspondent)

Sept. 3, 1938.

Congress of Public Health Physicians

Before the Congress of Public Health Physicians, in which all important interested officials of the national government were represented, Dr. Gütt, ministerial director from the national ministry of the interior, submitted an interesting report on the general state of public health. In recent years the agencies which protect the public health have been reorganized. There are today in Germany (exclusive of Austria) 753 health bureaus and 200 auxiliary centers. With these bureaus are affiliated ninety-five special departments of eugenics and racial hygiene. Full time employees of the public health services number 10,695, this number including the physicians and their trained and untrained assistants. There are 12,373 part time employees. Similar bureaus and centers are being established in Austria.

Dr. Gütt stressed the fact that leprosy, cholera, plague and smallpox can be considered as banished. On the other hand, the campaign against endemic contagious diseases is constantly confronted by new tasks, since the greater social contact and the assemblage of large groups, especially of children, have been accompanied by an increase in these infections. Thus diphtheria has been on the upgrade, although the disease has generally run a mild course. A reported total of 3,000 new cases of tuberculosis represents only an apparent increase, which is based on better detection of the disease by the anti-tuberculosis centers of the health bureaus. These centers cared for 1.5 million citizens during 1936. The tuberculosis mortality in 1937 in cities of 15,000 and more inhabitants reached a new low of 6.9 per 10,000 of population. The number of tuberculous children as reckoned on the basis of excuses from attendance at school has declined from the former proportion of between one half and two thirds to only one third. Sharp recessions have been noted in the morbidity and mortality of typhoid, paratyphoid and dysentery.

The health bureaus have likewise been engaged in energetic campaigns for nursing and infant welfare. In the year 1935, which marked the establishment of the new type of health bureau, 857,000 nurslings came under their care. Of a total of 1,276,000 babies born in Germany in 1937, no less than 1,129,000 received the services of the bureaus. The nursing mortality in the same year dropped to 6.4 per cent.

Dr. Gütt said that the problem of drug and food poisoning has not yet received adequate attention. In 1936, 6.4 milliards of reichmarks were spent for alcohol and tobacco. The damage which results hygienically, economically and socially from the misuse of these substances is generally underestimated.

As a consequence of the national genetic policy, the number of marriages in the larger cities increased from 609,000 in the year 1936 to 620,000 (9.2:1,000) in 1937. The present natality, according to an estimate of the national bureau of statistics, amounts to around 18.7:1,000 (as against 14.7:1,000 in 1933). The mortality seems to remain substantially unchanged. According to the expectation of life of particular age groups, the mortality of the entire German reich in 1936 should have reached 17.8:1,000 of population, whereas actually, thanks to improved hygienic conditions, the rate amounted to only 11.8. The danger of an aging of the German nation can carry with it the threat of a higher mortality. The existence of all European peoples is threatened to a greater or lesser degree, and now as before Germany is no exception. But the danger of race suicide is considerably greater in countries other than Germany.

Dr. Gütt concludes as follows: The greater the number of individual citizens of a nation who lead pleasant, irresponsible lives without regard to their own intrinsic value and biologic function and at the expense of the genetically sound and pro-

lific families, the sooner will the nation in question disappear from the family of nations. The democratic political philosophy, until recently accepted in Germany, favors just such a decline. Among the contributing factors to a dying-out of the most gifted and valuable members of society are celibacy, bachelorhood, homosexuality and advanced age at marriage of precisely the best-educated and most socially fit classes of society. If this trend were allowed to continue unchecked the white peoples and especially those of Germanic stock would become unfit to compete with other races in the biologic struggle for survival. Therefore, eugenics should be the cornerstone of a national political philosophy.

Prof. Paul Strassmann Is Dead

The illustrious Berlin gynecologist Prof. Paul Strassmann died recently at Gstaad, Switzerland, at the age of 72, after a brief illness. With him passes a most valuable contributor to the science and practice of his specialty. Strassmann came of an old Berlin family which had produced a whole series of distinguished physicians. He enjoyed an excellent training as assistant to Löhlein at Giessen, spent two years of study in England and returned to work for eight years with Gusserow in Berlin (at the Charité clinic). Later he established his own clinic, which came to be highly regarded. Strassmann's scientific contributions to obstetrics were numerous and valuable. In 1911 he received the degree of doctor honoris causa from the University of Birmingham. He was an honorary member of the St. Louis Gynecologic Society and corresponding member of the gynecologic society in Rome. His likable personality was everywhere esteemed.

BUCHAREST

(From Our Regular Correspondent)

Sept. 13, 1938.

Exanthematous Typhus in Bessarabia

M. Smadu, chief superintendent of health affairs in Bessarabia, has made a study of the causes, treatment and prevention of exanthematous typhus. This disease can be traced back to 1904, when it became epidemic. In 1919, 50,400 cases were recorded; in 1920, 31,246; in 1921, 3,486; in 1922, 2,196; in 1923, 3,347; in 1924, 2,217; in 1930, 1,140; in 1931, 951; in 1932, 1,313; in 1933, 1,225; in 1935, 2,400; in 1936, 4,227, and in 1937, 3,690. Thus typhus spent its fury after the war, then assumed a milder form and in the last three years appeared in a more vehement form as a consequence of bad economic conditions. The population, so to speak, marched out from the villages looking for food in distant regions. Such an exodus involved negligence of hygiene. The decrease in the number of cases in 1937 is attributable to the activities of the thirty-eight health detachments. The regular public health personnel is unable to spare time for the destruction of vermin in the houses. The area covered by the district physicians is in some cases huge and the roads in Bessarabia are almost impassable; thus the infection spreads rapidly. The detachments set up many disinfecting ovens and baths and taught the population how to live hygienically. The result was a decrease in the number of cases in 1937. Besides these detachments, seventy-seven young physicians were placed in service in the campaign. Three years ago a law was passed by the chamber of deputies according to which the compulsory military service of medical students lasts a year, half of which must be spent in the country.

The detachments were supplied with cauldrons for washing clothing and with irons, razors and hair-cutters. As there was a great shortage of underwear the ministry of health distributed 17,000 shirts among the poor. This gesture reduced the aversion of the population toward the detachments. The deparasiting detachments disinfected 182,774 houses and deloused 751,710 inhabitants.

The public health personnel of Bessarabia prior to the war consisted of 112 district physicians, 203 subordinate officials and eighty graduated midwives. Immediately after Bessarabia joined Rumania, the public health ministry increased the number of physicians to 207, that of the subordinate officials to 302 and that of the midwives to 136. Three years ago independent health inspectorates were established in seven counties of Bessarabia. It is necessary, says M. Smadu, that in every village at least one subordinate health official be engaged. In many communities there are a great number of families who do not know what soap is, and lack of personal cleanliness is a potent factor in the spread of exanthematous typhus.

According to M. Smadu, the campaign against exanthematous fever can be successful only if the whole population of Bessarabia is simultaneously subjected to deparasitation. He ordered the conscription of all clergymen, teachers, officials, public health subordinates and midwives, and in the nine districts found 9,300 such persons who will work in the service of deparasitation twice annually for six days without compensation. Their tasks are to supervise the population of the village, exert an influence from a hygienic point of view and deparasite the homes. M. Smadu proposed to the minister of culture that he instruct the 4,300 teachers of Bessarabia's children to instruct the rural population in personal cleanliness. In one village of the county of Cetatea Alba, with a population of about 5,800, more than 3,000 inhabitants were suffering from scabies, and the fourteen teachers of the village left the whole deparasiting work on the shoulders of the subordinate health official.

M. Smadu introduced two annual cleaning weeks, one before the Easter holidays and the other in October. Observance of these weeks is enforced by the clergymen, teachers, notaries public, subordinate officials and midwives. Great attention is given also to personal deparasitation. Doubtless at the beginning of this campaign the deparasiting was not perfectly done, but from 50 to 70 per cent of the population yielded to the requirements. Conscientious work carried out for a few years not only will exterminate exanthematous typhus but at the same time will accustom the rural population to cleanliness and hygienic living.

SWITZERLAND

(From Our Regular Correspondent)

Sept. 1, 1938.

The International Congress of Physiologists at Zurich

The sixteenth International Congress of Physiologists was held at Zurich August 14-19. Prof. W. R. Hess, Zurich physiologist, presided. It was especially appropriate that this meeting should take place in Switzerland, for this year the fiftieth jubilee of such congresses was celebrated and their origin under Swiss auspices was recalled. It was in 1888 that Friedrich Miescher, the renowned professor of physiology at Basel, invited physiologists of all lands to a first international assembly in Basel University's Institute of Physiology, only just opened at the time. The idea of arranging an international meeting of physiologists in Switzerland was suggested to Miescher by the British Physiological Society. The first congress was held Sept. 10-12, 1889, at Basel. Since that time the attendance at the congresses has increased nearly tenfold. At the 1889 congress many contributions of scientific importance were made. To mention a few of the more noteworthy: Von Mering and Minkowski submitted their classic studies of the pancreas; Mosso exhibited his ergograph, Goltz his decerebrized dog and Waller the first electrocardiogram, and Horsley demonstrated the motor functions of the cerebral cortex in apes. An account of the international congresses, which one might say is at the same time a history of the advances in physiology, is contained in a handsome commemorative volume, which the Physiological Society of England dedicated to the Swiss National Committee

apropos of the Zurich congress and a copy of which was presented to each participant. (Franklin, K. J.: *A Short History of the International Congresses of Physiologists*, *Ann. Sc.* 3:15 [July] 1938). Another recent commemorative work was the animatedly written, beautiful homage volume dedicated by the Swiss physiologists to Albrecht von Haller, the great Swiss physiologist of the eighteenth century. The author of this work was Johannes Strohl.

The first congress at Basel, in 1889, was attended by 129 scientists; more than 1,200 attended this year's meeting. At the 1889 congress twenty-five papers were read and twenty-three demonstrations performed; in Zurich this year the discussions and demonstrations numbered about 600. These statistics give some idea of the concentration necessary to assure smooth functioning of the transactions of the 1938 congress, as well as of the huge tangle of organizational problems which it befell the president, Professor Hess, and the secretary general, Prof. Ernst Rothlin (Basel) to unravel. Every country in the world in which the serious study of physiology is pursued was represented at the Zurich congress. The Americans present submitted an impressive series of papers. The congress performed a particularly valuable service in that through a large number of so-called arrangements of discussion important problems that claim the attention of the scientific world were introduced by authoritative workers in the field and thus opened to general discussion. It was in these discussions that the 1938 congress attained a level superior to that of any previous congress.

TOPICS

The following list of the more important topics and the men who introduced them offers a general idea of the ground covered by the congress: Functions of the different parts of the renal excretory system, A. N. Richards of Philadelphia and Brandt Relberg of Copenhagen; interrelation of local metabolism and circulatory regulation, Rein of Göttingen and Fleisch of Lausanne; cholinergy and adrenergic, Bacq of Liège and G. L. Brown of London; hydration of the animal organism and the physiologic reversibility of oxidative abba reactions, Knoop of Tübingen and Szent-Györgyi of Szeged, Hungary; permeability of the skin to medicaments and poisons, Flury of Würzburg and Bürgi of Berne; cellular parameter and the regulation of stimulus, K. S. Cole of Columbia University, New York, and Lullies of Cologne; effective substances of the sterol series, E. Laqueur of Amsterdam; respiratory problems of fetal life, Barcroft of Cambridge and Roos of Utrecht; problems of national nutrition, Abderhalden of Halle and Quagliariello of Naples; reflex regulation of respiration, Heymans of Ghent, Belgium, and R. A. Gesell of Ann Arbor, Mich.; the adrenal cortex, E. C. Kendall of the Mayo Foundation, Rochester, Minn., and Verzár of Basel; the hormone of the anterior lobe of the hypophysis, Houssay of Buenos Aires and K. J. Anselmino of Elberfeld; yellow respiratory ferment (vitamin B₂), Theorell of Stockholm and H. Chick of London; potential toxic effects, Tiffeneau of Paris and Gremels of Marburg.

The general discussion of a particular theme was in each instance begun by a notable contributor. The administration attempted in every possible way to effect a helpful collaboration between scientists from far-flung lands. The scientists were made conversant beforehand with the full program of the congress. To the printed program (of some 130 pages) was appended a series of abstracts of the individual reports prepared by the authors, and in addition each participant received two volumes entitled "Congress Reports I and II," which contained two indexes, one (71 pages) to the reports which were to introduce various topics of discussion and the other (394 pages) to the demonstrations and individual lectures. These preliminary measures placed the transactions on a sound basis and contributed to the scientific success of the

congress. Supplementary printed matter was run off from day to day. Unfortunately, the large number of master topics necessitated the holding of frequent parallel sessions. Four or more reports were sometimes read simultaneously to different sections. The spacious new home of the Confederate Institute of Technology was placed at the disposal of the congress, and the simultaneous discussions could there be held in adjacent rooms. As the demonstrations took place in part in this building and in part in nearby quarters, one could get about easily from one exhibit to another. Many of the demonstrations, including the motion picture exhibits, were repeated several times. Consequently in the course of those crowded days, every physician had an opportunity to attend the demonstrations that most interested him.

SESSION FOR PHARMACOLOGISTS

As everybody knows, the pharmacologists have to date never held an international congress of their own, although efforts to bring about such a meeting have been under way for some time. Accordingly pharmacologists in large numbers appeared at the congress of the sister science physiology. Many themes of discussion pertained to the province of pharmacology. At one entire afternoon session, completely given over to the pharmacologists, the chief topic was "The Scope and Future of Pharmacology." Introductory papers were read by Sir Henry Dale, London, and Prof. Walter Straub, Munich. At the end of this session the question of an international nomenclature was discussed and the present inconvenience of a plurality of names for single pharmaceutical substances deplored. Prof. Wolfgang Heubner, Berlin, was the principal speaker on this topic. The discussion was concerned with strictly scientific terms and not at all with the nomenclature of proprietary products. One gained the impression that the question of nomenclature will in future receive greater consideration.

RESULTS

On the whole, the 1938 congress provided a highly instructive cross section of our knowledge of the field of physiology. Its scientific mission may be said to have been fulfilled, but it served another purpose as well: greater personal collaboration among scientists. Such a collaboration has a twofold value. There is the human interest value incident to personal acquaintance with colleagues in one's own specialty, and there is the more practical consideration that problems may be elucidated and misunderstandings composed much more readily through personal contact and discussion than through the less direct avenues of correspondence and publication. For the promotion of a feeling of personal collaboration, such an important function of these congresses, the Swiss committee had planned the most elaborate facilities; these were taken advantage of by large numbers of the visitors and well served their purpose. The general feeling at the conclusion of the convention was appreciation for the work of the Swiss officials in this regard. At the final session complete satisfaction with the organization arrangements was expressed. On the invitation of the Physiological Society of England it was decided to hold the next congress in that country three years hence, at London, Oxford or Cambridge. The congress voted the establishment of a permanent international secretariat of physiologists to be located in Switzerland. This bureau, for which the Association of Swiss Physiologists has assumed responsibility, is designed to facilitate the administrative details of future congresses and to maintain closer relations between the various national societies of physiologists.

CONGRESS ON ALTITUDE PHYSIOLOGY

After the Zurich congress, the physiologists particularly interested in the problems of the physiologic reaction to high altitudes held a "Congress on Altitude Physiology." This meeting was held on the ridge of the Jungfrau; ninety scientists took part.

Prof. Alexander von Muralt, Berne physiologist, presided. Discussion was elicited by reports on various topics: the effects of altitude on the respiration, the circulation and the blood; mountain climate, the formation of snow and ice, a research expedition into the Chilean Andes and the physiologic station on Mount Etna. In addition there were demonstrations at the Jungfrau-Ridge High Alpine Research Station and motion pictures.

PALESTINE

(From a Special Correspondent)

TEL-AVIV, Aug. 23, 1938.

Medical Progress in Palestine

Before the outbreak of the World War, modern standards of medical practice and hygiene were practically unknown in Palestine. To the Arab but one disease was known, "harrara," a term for all communicable diseases, including malaria, and all infections of the eyes. Since in most cases conditions diagnosed as conjunctivitis were in reality trachoma, "harrara" might also indicate the presence of this infection. Similarly, all serious infections of the skin were called "harrara." At the time of the British occupation, there were only a handful of physicians in the country, and but few of them had enjoyed the advantages of medical training in Europe. Hospitals were in an equally backward state. They had been founded by missionary societies and were utterly lacking in modern facilities. The superintendent not only was engaged in administration but was at the same time internist, surgeon and gynecologist. With the cessation of hostilities, Jewry turned to Palestine and a steady stream of young progressive elements began to pour into the country. They came first in small groups from Central and Eastern Europe and later in larger numbers from both Eastern and Western Europe, bringing with them standards of medical aid, which they wished to embody at once in their "new homeland."

MEDICAL WORK OF HADASSAH

The Women's Zionist Organization of America, Hadassah, which today numbers 60,000 members, made possible the organization of medical aid on a modern basis. The medical activities of this organization, begun in 1913, were abruptly curtailed by the outbreak of the war. In response to an appeal from the World Zionist Center in London, Hadassah undertook to send a medical expedition to Palestine. The first American Zionist medical unit, composed of doctors, nurses, bacteriologists and sanitary engineers, arrived in 1918, while war was still being waged in the country. This unit began at once to combat epidemic diseases, especially malaria. A chain of dispensaries was opened in towns and colonies. Hospitals were established in Jerusalem, Tel-Aviv, Haifa and Safad. Infant welfare stations were set up in every part of the country and their services extended free of charge to all, regardless of race or creed. School hygiene was introduced, with special emphasis on dermatologic and ophthalmic treatments. The spread of communicable diseases was combated with success, and improved standards of hygiene were introduced into the home. When Hadassah began its work the incidence of trachoma was high. Owing to intensive treatment the rate in the Jerusalem schools was reduced from 21.6 per cent in 1918 to 3.27 per cent in 1935. The efforts of the first Hadassah sanitary squad have been vastly enlarged. Extensive antimalaria drainage has been carried out in cooperation with the Jewish National Fund and the Palestine Jewish Colonization Association ("Pica"), and malaria-ridden districts have been reclaimed for colonization.

It was apparent that an inexperienced community absorbed in intense upbuilding could not yet maintain an effective medical system without outside aid. From the outset it was a part of Hadassah policy to initiate new enterprises and continue their maintenance only until the work was justified in the eyes of the public and the community was able to assume financial responsibility. With the growth of the Jewish community and the

improvement in its economic conditions, Hadassah began a program of transferring its institutions to local bodies. The work was begun with the transfer of its hospitals outside Jerusalem. Transfer of health, welfare and rural medical services followed. These services were concentrated in a newly organized rural insurance institution, known as the Kupat-Holim-Amamit, which extends its benefits to farmers and other elements not affiliated with the General Federation of Jewish Labor. This assumption of responsibility by local communities is enabling Hadassah to fulfil its original purpose, the founding in Palestine of that which is beyond the resources of a relatively small and pioneer community. Under these circumstances, Hadassah, in cooperation with the American Jewish Physicians' Committee under the leadership of Dr. Ratnofsky, has undertaken to establish a medical center on Mount Scopus.

COOPERATIVE SCHEMES FOR MEDICAL AID

Jewish pioneers who had come to Palestine to remold their lives could not become passive recipients of medical aid. Even before the arrival of the Hadassah medical unit they had initiated cooperative schemes for medical aid. These independent efforts were continued until they succeeded in developing an important health insurance organization, Kupat-Holim of the General Federation of Jewish Labor in Palestine. From a membership of 2,000 in 1929 the organization has made rapid strides and today numbers 75,000. Including members' dependents, it provides medical service for about 140,000 persons, or about one third of the total Jewish population of Palestine. In a country in which no compulsory health insurance legislation has been enacted this is truly remarkable. While agricultural workers were the founders of the organization, today its ranks embrace skilled and unskilled workers in town and village, workers in every branch of industry and public works, clerical workers and members of the liberal professions. The benefits of the service have augmented its membership from year to year and have gained the cooperation of an increasing number of employers who pay their contributions of their own volition. In various undertakings employing both Jews and Arabs this contribution is paid, and all workers, including hundreds of Arab laborers, enjoy its institutions. The rural dispensaries of Kupat-Holim and Hadassah have always extended aid to the Arabs of the district. It was at one time not uncommon for whole families to trail tens of miles for treatment during the summer, when epidemic diseases are prevalent. These rural medical centers not only treated the sick and ailing but endeavored to teach the principles of hygiene to wandering Bedouins and peasants, hitherto healed by the charms of the medicine man.

The workers' health insurance organization, Kupat-Holim, conducts 165 dispensaries; three central dispensaries in the principal cities; two hospitals, one in the Valley of Jezreel and one in the Sharon, near Petach-Tikva, and two convalescent homes, one on Mount Carmel and one in the Judean hills near Jerusalem. Pharmacies are attached to its rural and urban dispensaries; modern x-ray machines are installed in its central dispensaries and hospitals; physical therapy clinics and a central analytic laboratory provide its members with special services. It employs 300 physicians, most of whom have come from Europe, 200 nurses, forty dentists, thirty-five pharmacists and a large staff of clerical and technical assistants. The Jewish health enterprises herein described were initiated and developed independently by various organizations. In time it became apparent that the coordination of their activities demanded a central body. This need found expression in the establishment of a health council, consisting of seven members and four ex officio members; the directors of the Hadassah medical services, of the workers' health insurance organization and of the rural insurance society, and a representative of the municipality of Tel-Aviv. This council fulfils various functions for the community as a whole.

Hospital Service

Most of the hospital care in Palestine is provided by voluntary agencies and municipal bodies.

The workers' health insurance organization accompanied the pioneer to outlying, malarial areas, where he was breaking ground for new settlements. At the first cooperative settlement established in the Valley of Jezreel, at Ain Harod, the first hospital unit was opened in 1923, in huts under primitive conditions. The first permanent buildings of the hospital were erected in 1929, and various units have since been added. The hospital lies in the heart of an agricultural area and was intended for the labor settlements of Lower and Upper Galilee. As it was for years the only hospital with a well equipped medical section, patients were sent from Haifa as well as from Galilee. Similarly, its gynecologic, maternity and pediatric wards were forced to admit patients from the Haifa district. The enlargement of its x-ray department and the acquisition of an electrocardiograph during the past year have provided modern diagnostic facilities for the hospital as well as for the dispensaries of the vicinity. The hospital has sixty beds and its records show a 100 per cent occupancy in 1937. During this period 2,018 patients were admitted, representing 25,911 sick days, or an average of 12.8 days per patient. The hospital is faced with two main difficulties. Since it lies in a new colonization area, the scope of its jurisdiction is being constantly enlarged and not infrequently by the addition of malaria-infected areas. It is greatly handicapped by the lack of a proper surgical department. Emergency cases are treated, but all transportable patients are referred to the nearest surgical department at Haifa. This is at no time advisable and is fraught with danger in view of the present unrest in the country. Political upheavals in recent years have restricted the opportunities for graduate study abroad. Such study has been in part replaced by an intensive program of clinics and conferences in which local specialists as well as visiting physicians from abroad have participated. The Afulah branch of the Julius Jarcho Medical Library of the Hebrew University has been transferred to the hospital and provides the physicians of both the hospital and the district with modern medical books and periodicals.

The second hospital of the workers' health insurance organization, the Belinson Hospital, opened in October 1936, is situated on the Petach-Tikva Road about ten miles from Tel-Aviv in the heart of a citrus fruit area. The following units have been completed: (1) a 100 bed hospital containing four wards (medical, surgical, gynecologic-obstetric and pediatric), operating and supply rooms, an x-ray division, a laboratory and a small pathology building; (2) housekeeping and service rooms, and (3) quarters for the physicians, general staff and persons in training. The construction of the present buildings entailed an expenditure of £P. 50,000, of which £P. 8,000 was contributed by the Palestine government and the balance raised by Kupat-Holim. An unusual shortage of beds and the suffering thereby entailed for its members forced the workers' organization (which is not a publicly supported institution) to undertake the construction and maintenance of this institution. The demand for hospitalization has been beyond its capacity. The average daily occupancy for 1937 was ninety-eight (including that of the nursery, 120). The first half of 1938 showed an increase of 10 per cent. In consequence of this demand for beds only seriously ill patients are admitted.

Facilities for proper ventilation were provided in all the wards, and an air-conditioning plant was installed in the nursery; such facilities are of inestimable importance in our subtropical climate. The hospital has been fully equipped with modern facilities for diagnosis and therapy. The following apparatus was acquired during 1937: electrocardiograph, thoracoscope with thorac-acoustic attachment, gastroscope, Macknsson gas apparatus for administration of nitrogen monoxide-ether and a surgical diathermy machine. Operations on the nose, throat, ear and oral

cavity are performed by specialists. A few months ago a chest surgeon of long experience was attached to the staff, and special attention is being given to his division. Except the specialists mentioned, all physicians, including departmental heads, are on full time and in residence. An enlightened attitude on the part of the members makes possible autopsies and microscopic examinations of tissues for pathology. Pathologic specimens are being saved, and it is hoped in the course of time to build up a valuable collection. The nucleus of a medical library is found in the hospital. Thanks to the assistance of Dr. Jarcho of New York City, new books and some forty current periodicals are received regularly. Interesting cases are presented in weekly clinics, to which the physicians of the district dispensaries are invited. The Kupat-Holim School of Nursing is attached to the hospital. It was opened over two years ago and now has an enrolment of fifty-one.

THE MEDICAL CENTER OF THE HADASSAH UNIVERSITY HOSPITAL

The new medical center of the Hebrew University will consist of three units: the Rothschild-Hadassah University Hospital, the Henrietta Szold Hadassah School of Nursing and the Nathan Ratnoff Medical School.

The hospital will provide from 270 to 300 beds, and additional structures in the future will permit an optimum capacity of 500. European and American experience in hospital construction have been adapted to the needs of the country, and a building which stands out for the simplicity of its lines has been achieved. Modern improvements and developments have been fully provided for in the equipment. No ward is to contain more than five beds. Most rooms will contain but three beds, and a limited number of single and double rooms will be available. Kitchen, laundry and other facilities have been equipped with the latest apparatus. Laboratories and lecture halls provide special facilities for clinics, research and instruction. The hospital will contain the following departments: general, surgery, gynecology, ophthalmology, dermatology, neurology, cancer and a special maternity pavilion to be named in memory of Paulina Ratnoff. The buildings are to be surrounded by a garden overlooking the Hills of Moab and the Dead Sea to the east and to the west the old city of Jerusalem and the ancient seat of the temple.

The school of nursing will be housed in a three story building. Lecture halls and laboratories will be located on the ground floor. The second and third stories will contain dormitories for persons in training and for a small number of nurses. The school will continue to prepare fully qualified nurses for Hadassah and other medical institutions.

The three story medical school building will contain laboratories for clinical research, lecture rooms for hygiene, bacteriology, serology, parasitology, pathologic chemistry, pathology and cancer and hormone research laboratories. An additional story to be constructed will contain laboratories for physiology and pharmacology and other branches as required. The cost of the three units, including equipment, will amount to £P. 170,000. This amount has been raised by the American Committee for the Erection of Hospitals in Palestine, comprising representatives of Hadassah and the American Jewish Physicians' Committee. Hadassah will continue to manage the hospital and the school of nursing, while the university will organize the teaching and research work. A special preparatory committee, consisting of representatives of the university, of the Jewish National Council and of Hadassah, will deal with teaching and research problems so far as they concern both institutions.

Medical Activities of the Hebrew University

In 1925, when the Hebrew University was officially opened, plans were made for the establishment of a medical division. The American Jewish Physicians' Committee, under the chairmanship of Dr. Ratnoff, made possible the erection of a microbiology building and the establishment of a parasitology

department. In 1926 the medical committee of the joint distribution committee contributed the means for the department of hygiene and bacteriology. Dr. Kligler of Columbia University and the Rockefeller Institute, New York City, was summoned from Haifa, where he was at the time directing the government station for malaria research, to head the department. The departments are making progress and now have a staff of ten collaborators of scientific standing, as well as younger assistants and a technical personnel. The department of bacteriology and hygiene devotes itself primarily to serologic and epidemiologic questions as related to the epidemiology of malaria, and a special station for this purpose was established at Rosh Pinah. The department of parasitology, under Prof. Saul Adler, deals with medical entomology and helminthology. In the medical graduate school, the following professors have been appointed in the clinical departments: Dr. B. Zondek, gynecology, and Dr. Halberstaedter, radiology.

An anonymous gift received by the University in 1935 for cancer research made possible the establishment of two new departments, those of radiology and experimental pathology. Both laboratories are fully equipped with modern apparatus and are being housed in the Nathan Strauss Health Center until the completion of the medical center on Mount Scopus. A special roentgen ray apparatus has been set up which permits rays of varying wave lengths to be produced in exceptionally powerful doses. Special attention has been paid to the investigation of tumor-producing powers of rays and, on the other hand, to the possibilities of producing therapeutic effects on tumors by means of rays. The department of experimental pathology considers its chief task to be the study of physiologic processes leading to cell division. This study is based on "tissue culture." In addition, the department is investigating purely pathologic problems. Particular mention should be made of the study of leukemia, with special reference to the possibility of growing the virus of leukemia, and its relation to cancer-producing agencies.

In the past six years the university has taken measurements of the intensity of the sun's radiation in the mountain districts surrounding Jerusalem and occasionally on the shores of the Dead Sea and the Mediterranean. These experiments, which are unique in the Near East, have already revealed that the solar energy which reaches the earth is greatest on fine winter days and least on the hottest days of the year. Ultraviolet sun rays are being investigated at five different points. Part of the necessary means were put at the university's disposal by the Kupat-Holim.

Marriages

JOHN D. WORKMAN, Lake Worth, Fla., to Miss Edith Beatrice Burrell of Biltmore, N. C., at Jacksonville, Fla., August 22.

JOHN PIERCE LAMBERT, Scarsdale, N. Y., to Miss Catherine Grant Nelson of Rocky Mount, N. C., at Clayton, Ga., August 15.

ROBERT NELSON SMITH, Comanche, Texas, to Miss Elizabeth Ada Lambert of Montclair, N. J., September 24.

GRADY CORNELL SISKE, Pleasant Garden, N. C., to Miss Robbie Emily Dunn of Greensboro, August 22.

JOSEPH R. CATON, South Bend, Ind., to Miss Margaret McMeel of Great Falls, Mont., September 3.

JAMES V. SACCHETTI, Worcester, Mass., to Miss Kathryn R. Sacino of Fitchburg, June 22.

FRANK H. POWER to Miss Margaret Goodrich, both of Ann Arbor, Mich., July 30.

SAMUEL R. MERCER to Miss Helen Cooper, both of Fort Wayne, Ind., September 3.

MAXWELL D. FLANK to Miss Ada R. Schwartz, both of Brooklyn, August 28.

HERMAN WECHSLER to Miss Rosalind Stieglitz, both of New York, September 11.

Deaths

Alonzo Gale Howard ☉ Boston; Boston University School of Medicine, 1895; professor emeritus of orthopedic and fracture surgery at his alma mater; consulting orthopedic surgeon to the Massachusetts Memorial Hospitals; member of the American Academy of Orthopedic Surgeons; fellow of the American College of Surgeons; aged 68; died, July 4.

Morris Jacob Lesoff ☉ Far Rockaway, N. Y.; University of Vermont College of Medicine, Burlington, 1911; member of the Radiological Society of North America; on the staff of St. Joseph Hospital, Far Rockaway, South Nassau Communities Hospital, Rockville Center and the Meadowbrook Hospital, Hempstead; aged 53; died, July 2, of heart disease.

Maurice Edward Barron, Boston; Tufts College Medical School, Boston, 1914; member of the Massachusetts Medical Society; professor of clinical surgery at his alma mater; fellow of the American College of Surgeons; on the staff of the Beth Israel Hospital; aged 46; died, August 22, in Bristol, R. I., of coronary occlusion.

Harry Sands Weaver Sr., Philadelphia; Hahnemann Medical College and Hospital of Philadelphia, 1892; professor of laryngology, rhinology and otology at his alma mater; member of the Medical Society of the State of Pennsylvania; fellow of the American College of Surgeons; aged 70; died, July 7, of carcinoma of the bladder.

Nelson O. Brooks, Oncida, N. Y.; University of Buffalo School of Medicine, 1894; member of the Medical Society of the State of New York; member of the House of Delegates of the American Medical Association, 1917, 1918 and 1926; formerly city health officer and coroner; aged 70; died, July 5, of coronary thrombosis.

Joseph Wiener ☉ New York; College of Physicians and Surgeons, Medical Department of Columbia College, New York, 1893; fellow of the American College of Surgeons; on the staffs of the Mount Sinai Hospital, St. Joseph's Hospital and the Rockaway Beach (N. Y.) Hospital; aged 66; died, August 28.

Joseph Aladin Barre, Fall River, Mass.; College of Physicians and Surgeons, Baltimore, 1892; member of the Massachusetts Medical Society; at one time a member of the police board and of the board of health; on the staffs of the Union Hospital and St. Anne's Hospital; aged 69; died, July, 25.

Charles R. Ziegler, Carrollton, Ohio; Jefferson Medical College of Philadelphia, 1874; member of the Ohio State Medical Association; past president of the Carroll County Medical Society; county physician; aged 88; died, July 30, as the result of a fall suffered several months previously.

Henry D. Smith, Washington, Kan.; Lincoln Medical College of Cotner University, Lincoln, Neb., 1897; member of the Kansas Medical Society; president of the Washington County Medical Society; veteran of the Spanish-American and World wars; formerly mayor; aged 63; died, July 19.

Joseph James Scroggs, Beaver, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1902; member of the Medical Society of the State of Pennsylvania and the American Academy of Ophthalmology and Otolaryngology; aged 61; died, July 19, of cerebral hemorrhage.

Thomas Ellsberry Gray, Winslow, Ark.; Kansas City (Mo.) Medical College, 1901; member of the Arkansas Medical Society; served during the World War; lieutenant colonel in the medical reserve corps; for several years mayor and member of the city council; aged 64; died, July 11.

William B. Clapper, Victor, N. Y.; College of Physicians and Surgeons, Baltimore, 1894; member of the Medical Society of the State of New York; on the staff of the Frederick Ferris Thompson Hospital, Canandaigua; aged 73; died suddenly, July 22, of cardiac decompensation.

John Arnold Urner, Minneapolis; University of Minnesota Medical School, Minneapolis, 1924; associate professor of obstetrics and gynecology at his alma mater and the graduate school; aged 42; died, July 16, in the Minneapolis General Hospital of cirrhosis of the liver.

John Edgar Bowman ☉ Greenwich, Conn.; University of Toronto Faculty of Medicine, 1889; member of the Medical Society of the State of New York; medical superintendent and owner of a sanatorium bearing his name; aged 79; died, July 21, of carcinoma of the prostate.

Samuel Ashby Grantham Sr., Joplin, Mo.; Marion-Sims College of Medicine, St. Louis, 1892; member of the Missouri

State Medical Association; veteran of the Spanish-American War; on the staffs of the Freeman and St. John's hospitals; aged 72; died, July 31.

Angier Bailey Hobbs, New York; College of Physicians and Surgeons, Medical Department of Columbia College, New York, 1889; formerly medical director of the New York Life Insurance Company; aged 74; died, July 24, in Bronxville, N. Y., of heart disease.

Mayer Rosen, Philadelphia; Jefferson Medical College of Philadelphia, 1897; member of the Medical Society of the State of Pennsylvania; served during the World War; aged 62; died, July 5, in the Jewish Hospital of ruptured dissecting aneurism.

Isidore Andrew McClellan, Buffalo; American Eclectic Medical College, Cincinnati, 1880; Civil War veteran; aged 87; died, July 24, in the United States Marine Hospital of injuries received in a fall, hypostatic pneumonia and chronic myocarditis.

Elmer G. Starr, Pasadena, Calif.; University of Buffalo School of Medicine, 1884; fellow of the American College of Surgeons; formerly emeritus professor of ophthalmology at his alma mater; aged 77; died, July 21, of coronary occlusion.

Jacob John Kocher, Palm Springs, Calif.; Hahnemann Medical College and Hospital of Philadelphia, 1906; Jefferson Medical College of Philadelphia, 1907; aged 61; died, July 15, in the Palo Alto (Calif.) Hospital of coronary thrombosis.

Guy Frank Robinson, Livermore, Calif.; St. Louis College of Physicians and Surgeons, 1905; served during the World War; aged 54; on the staff of the Veterans Administration Facility, where he died, July 15, of general peritonitis.

Thomas Robert Durkin Jr., Philadelphia; Georgetown University School of Medicine, Washington, D. C., 1936; resident to St. Vincent's Hospital; aged 27; died, July 5, in St. Agnes' Hospital of subacute bacterial endocarditis.

Kallman Meyer Davidson ☉ Boston; Albertus-Universität Medizinische Fakultät, Königsberg, Prussia, 1887; fellow of the American College of Physicians; on the staff of the Beth Israel Hospital; aged 76; died, July 22.

Benjamin J. High, Elmwood, Tenn. (licensed in Tennessee in 1891); formerly secretary of the Smith County Medical Society; aged 75; died, July 31, in the Central State Hospital, Nashville, of chronic myocarditis.

Thomas Joseph Cahill ☉ Cambridge, Mass.; Tufts College Medical School, Boston, 1907; served during the World War; on the staff of the Cambridge City Hospital; aged 54; died, July 4, of coronary occlusion.

B. Ethelbert Watterson, Continental, Ohio; Ohio Medical University, Columbus, 1902; member of the Ohio State Medical Association; for many years member of the board of education; aged 69; died, July 3.

James Hunter Wells, Portland, Ore.; University of Oregon Medical School, Portland, 1888; at one time a medical missionary; formerly city health officer; aged 72; died, July 3, in the Emanuel Hospital.

Robert Warren Ramsay ☉ Littlestown, Pa.; Jefferson Medical College of Philadelphia, 1886; an Affiliate Fellow of the American Medical Association; aged 79; died, July 18, of cerebral hemorrhage.

Albert Alonzo Tennant, Richmond, Va.; Leonard Medical School, Raleigh, N. C., 1904; aged 59; medical superintendent of the Richmond Community Hospital, where he died, July 12, of heat prostration.

Joseph Le Roy Stevens, Dayton, Ohio; University of Cincinnati College of Medicine, 1932; member of the Ohio State Medical Association; aged 39; was killed, July 31, in an automobile accident.

Marcus Benjamin Halpern, Newark, N. J.; Hospital College of Medicine, Louisville, Ky., 1906; aged 64; died, July 9, at St. Barnabas Hospital of cardiovascular renal disease and arteriosclerosis.

Charles Rea Dickson, Toronto, Ont., Canada; Queen's University Faculty of Medicine, Kingston, 1880; University of the City of New York Medical Department, 1881; aged 79; died, July 9.

John Lawson Norris, Hendersonville, N. C.; National University Medical Department, Washington, D. C., 1897; served during the World War; aged 64; died, July 28, of coronary thrombosis.

Harry S. Wolff, Memphis, Tenn.; Missouri Medical College, St. Louis, 1898; house physician to the B'nai B'rith Home; aged 67; died, July 26, of diabetes mellitus and angina pectoris.

William Davies Gibbon, Dunbar, Neb.; Sioux City (Iowa) College of Medicine, 1895; aged 64; died, July 5, in Rancho Santa Fe, Calif., of coronary sclerosis, duodenal ulcer and pyloric stenosis.

Milton L. Snyderman, Philadelphia; Temple University School of Medicine, Philadelphia, 1937; intern at the Mount Sinai Hospital; aged 25; died, July 11, of Hodgkin's disease.

Robert Toru Masuhara, Ann Arbor, Mich.; University of Michigan Medical School, Ann Arbor, 1935; aged 30; died, July 7, in the University Hospital of military tuberculosis.

Henry Tucker, Bellevue, Md.; Jefferson Medical College of Philadelphia, 1894; served during the World War; aged 67; died, July 19, of angina pectoris and arteriosclerosis.

Derk Mulder, Lynden, Wash.; Universiteit van Amsterdam Geneeskunde Faculteit, Netherlands, 1881; College of Physicians and Surgeons of Chicago, 1887; aged 76; died, July 3.

James Porterfield Hull Ⓢ Stockton, Calif.; University of California Medical Department, San Francisco, 1895; aged 66; died in July, of arteriosclerosis and coronary occlusion.

John Esler, Cereel, Alta., Canada; University of Toronto Faculty of Medicine, 1902; medical superintendent and owner of the Cereel Hospital; aged 60; died, in July.

Andrew J. Wood, Macon, Ga.; University of Georgia Medical Department, Augusta, 1881; aged 84; died, July 16, in the Macon Hospital of pulmonary tuberculosis.

Roy Oscar Miller, New York; University of Toronto Faculty of Medicine, 1911; aged 55; died, July 31, in Jersey City, when he fell from a third story window.

Monroe De Tar, West Palm Beach, Fla.; Medico-Chirurgical College of Kansas City (Mo.), 1901; aged 76; died, July 15, of acute dilatation of the heart.

Charles Belton Macartney, Thorold, Ont., Canada; Detroit College of Medicine, 1903; Queen's University Faculty of Medicine, Kingston, 1911; aged 62; died, July 27.

Jehu Franklin McCool, Boonville, Ind.; Indiana University School of Medicine, Indianapolis, 1909; served during the World War; aged 56; died, July 23, of pneumonia.

Feibisch Rukhaus Ⓢ Cleveland; Medizinische Fakultät der Universität Wien, Austria, 1924; aged 43; died, July 12, of an overdose of a narcotic, self administered.

John Thomas Martin, Battle Creek, Mich.; University of Louisville (Ky.) Medical Department, 1905; aged 57; died, July 30, of chronic intestinal obstruction.

Bishop Marvin Kendrick, Luverne, Ala.; Medical College of Alabama, Mobile, 1903; aged 60; died, in July, at a hospital in Montgomery of sclerosis of the liver.

Malcolm L. Jackson, Spicewood, Texas; University of Tennessee Medical Department, Nashville, 1894; aged 71; died, July 28, of carcinoma of the stomach.

Alfons Ludwig Hageboeck Ⓢ Davenport, Iowa; State University of Iowa College of Medicine, Iowa City, 1889; aged 71; died, July 28, of cerebral embolism.

Ono Polk Sala Ⓢ Davenport, Iowa; Milwaukee Medical College, 1897; formerly on the staff of the Mercy Hospital; aged 65; died, July 21, of angina pectoris.

James B. Bridges, Seattle; Rush Medical College, Chicago, 1882; member of the Missouri State Medical Association; aged 81; died, July 22, of arteriosclerosis.

Joseph Martin Swindt Ⓢ Chino, Calif.; Cornell University Medical College, New York, 1932; aged 32; was found dead, July 11, of poison, self administered.

Horace Ivey Thomson, St. Petersburg, Fla.; Chicago College of Medicine and Surgery, 1916; served during the World War; aged 45; died in July.

Carl Braun Groschner, Toledo, Ohio; Jefferson Medical College of Philadelphia, 1897; aged 64; was found dead, July 28, of a self-inflicted bullet wound.

Allen Harris Peek, Ventura, Calif.; Cooper Medical College, San Francisco, 1904; aged 60; died in July of illuminating gas poisoning, self administered.

John Tolson, Church Point, La.; University of the South Medical Department, Sewanee, Tenn., 1904; aged 55; died, July 18, of cerebral hemorrhage.

Louise Norton Lenman, Washington, D. C.; Washington (D. C.) Homeopathic Medical College, 1896; aged 67; died, July 17, of coronary occlusion.

Joel E. Luther, Mountain View, Ark.; Arkansas Industrial University Medical Department, Little Rock, 1897; aged 70; died, July 28, of heart disease.

Richard W. St. Benno, Glen Ellyn, Ill.; College of Medicine and Surgery Chicago 1910; aged 54; died, July 19, of valvular heart disease and nephritis.

William Fankuchen, Brooklyn; Long Island College Hospital, Brooklyn, 1902; aged 59; was found dead, July 27, of morphine, self administered.

Frederick Eiche, Lincoln, Neb.; Northwestern University Medical School, Chicago, 1903; aged 72; died, July 12, in the State Hospital of senility.

Fernando Aguilar, Albany, N. Y.; New York Medical College and Flower Hospital, New York, 1917; aged 57; died, July 26, of cholelithiasis.

W. George Meredith, Tewksbury Township, N. J.; Homeopathic Hospital College, Cleveland, 1886; aged 77; died, July 10, of chronic myocarditis.

Adam D. Blomeyer, Cape Girardeau, Mo.; Beaumont Hospital Medical College, St. Louis, 1891; aged 72; died, July 22, of cerebral hemorrhage.

Edwin A. Wilson Ⓢ Salem, W. Va.; Cincinnati College of Medicine and Surgery, 1898; aged 72; died, July 12, of coronary thrombosis.

Arthur Nelson Rowe Ⓢ Newport, Wash.; Rush Medical College, Chicago, 1913; aged 59; died, July 20, in Tucson, Ariz., of bronchial asthma.

John R. Moore, Coushatta, La.; Memphis (Tenn.) Hospital Medical College, 1895; aged 72; died, July 17, of thromboangiitis obliterans.

William Walter Latham Ⓢ Madisonville, Texas; Memphis (Tenn.) Hospital Medical College, 1896; aged 64; died, July 28, of angina pectoris.

John Corran McCauley Sr., Rochester, Pa.; Western Homeopathic College, Cleveland, 1890; aged 73; died, July 19, of arteriosclerosis.

Thomas George Loudon, Peterborough, Ont., Canada; Queen's University Faculty of Medicine, Kingston, 1919; aged 54; died, July 6.

James Henry Hinchcliffe, Philadelphia; Medico-Chirurgical College of Philadelphia, 1903; aged 63; died, July 28, of heart disease.

M. C. Smith, North Girard, Pa.; College of Physicians and Surgeons, Baltimore, 1887; aged 73; died, July 5, of diabetes mellitus.

James A. Ryan, Oklahoma City; Hospital College of Medicine, Louisville, Ky., 1887; aged 81; died, July 12, of carcinoma of the prostate.

Isaac W. Costen, Roanoke, Va.; College of Physicians and Surgeons, Baltimore, 1892; aged 70; died, July 1, of cerebral hemorrhage.

Oscar J. Jordan, Philadelphia; Hahnemann Medical College and Hospital of Philadelphia, 1890; aged 73; died, July 11, of heart disease.

Otto Paul Ludwig, Chicago; Milwaukee Medical College, 1909; aged 53; died July 25, of cerebral hemorrhage and hypertension.

James Carter Giles, Danville, Va.; University College of Medicine, Richmond, 1903; aged 62; died, July 29, of myocarditis.

James Eliakim Patrick, Bahama, N. C.; University College of Medicine, Richmond, 1900; aged 67; died, July 28, of myocarditis.

John Thomson Green, Hamilton, Ont., Canada; Western University Faculty of Medicine, London, 1912; aged 50; died, July 13.

R. T. Madison, Amorita, Okla.; College of Physicians and Surgeons, Keokuk, Iowa, 1876; aged 85; died, July 6, of senility.

Frederic Bacon Cullens, Ozark, Ala. (licensed in Alabama in 1897); aged 74; died, July 12, of heart disease and nephritis.

H. Earl Coger, Houston, Texas (licensed in Texas, under the Act of 1907); aged 64; died, July 30, of heart disease.

Harry Weldon Osgood, Bangor, Maine; Boston University School of Medicine, 1898; aged 67; hanged himself, July 5.

David O'Shea, Chicago; Rush Medical College, Chicago, 1883; aged 83; died, July 24, of carcinoma of the rectum.

L. A. Parks, Lancaster, Ohio; Starling Medical College, Columbus, 1882; aged 80; died, July 1, of pneumonia.

William H. Riley, Ridgway, Ill.; Eclectic Medical Institute, Cincinnati, 1880; aged 82; died, July 26, of malaria.

Ernest H. A. Allison, Denver; Denver College of Medicine 1893; aged 84; died, July 30.

J. G. Goodner, Georgetown, Tenn. (licensed in Tennessee in 1889); aged 79; died, July 10.

Bureau of Investigation

CHROMARAY—TRIORAY

The Therapeutic (?) and Commercial Possibilities of Color

Chrome-Therapy—or, to use plain English—"cure by colored lights," like most forms of modern quackery or faddism, plays on the public's little knowledge that proves so dangerous when applied to the treatment of human ailments. The nonmedically trained person has hazy—and usually erroneous—notions of the therapeutic value of ultraviolet and infra-red rays; he has equally vague ideas of the place that heliotherapy—sun treatment—plays in the treatment of disease; he has a dim recollection of what he learned about the spectrum when he attended classes in high-school physics. With these scraps of knowledge floating hazily within his cerebral horizon, what more plausible than the claims set forth in ponderous seriousness, whether by enthusiastic faddists or venal quacks, that human pathology is in some way due to "a disturbance of Color balance" or that it can be cured by restoring "Radio-Emanative Equilibrium by Attuned Color Waves"—whatever such verbal pyrotechnics may mean!

The commercial possibilities of the use of color as a "patent medicine" have been appreciated by various faddists and quacks for some time. The "Bio-Dynamo-Chromatic Diagnosis" of quack George Starr White; the "Chromo Therapy and Diagnosis" of America's most accomplished charlatan, Albert Abrams, immediately come to mind as two of the many cults that tilled this lush field. Then came Dinshah P. Ghadiali and his "Spectro-Chrome Therapy," Karl von Schilling's "Vita Chrome" and now the "Chromaray" and "Trioray" of E. A. Ernest of the Ernest Distributing Company of Milwaukee.

Mr. Ernest should be well qualified to expound the commercial possibilities of the spectrum. He might paraphrase by declaring, "Thar's gold in them thar colors!" A few years ago the Ernest Distributing Company described itself as the "Exclusive United States Distributors for Spectro-Chrome Equipment." It handled the fantastic gadgets put out by Dinshah P. Ghadiali, who has exploited Spectro-Chrome Therapy continuously for years—save for a period when he was serving a term in a federal penitentiary for violation of the Mann Act.¹

Ghadiali's thesis was that in health the preponderating color-waves of the elements in the human body—oxygen, hydrogen, nitrogen and carbon—are "in balance." When they get "out of balance" the human body is diseased; *ergo*, to cure disease, administer the colors that are lacking or reduce the colors that are too brilliant! According to Ghadiali, yellow light aids digestion, kills worms and builds nerves; violet depresses the heart; orange will cause vomiting; blue will build vim, vigor and vitality. And so on!

In the autumn of 1933 a Wisconsin newspaper, the Milwaukee *Journal*, conservatively described the Ghadiali gadgets, handled by Ernest, as "hocus-pocus." It was reported that Ghadiali threatened to sue the newspaper unless a retraction was made. While Ghadiali's bark is most ferocious and awe-inspiring, his bite is toothless. No retraction was made and Ghadiali brought no suit. Ernest, however, filed suit for libel against the paper, asking \$150,000 damages and \$35,000 special damages. This in spite of the fact that the *Journal* did not mention Ernest by name in its article. When the suit came to trial, the jury decided that the Milwaukee *Journal* was fully justified in characterizing Ghadiali's gadgets as quackery.

Later Mr. Ernest ceased acting as "exclusive distributor" of the Ghadiali devices, and by November 1937 he and Ghadiali had so far parted company that the latter brought an action in equity against Ernest, charging him with an infringement of a patent granted Ghadiali in 1925 for "certain new and useful improvements in color wave projection apparatus." It is a fact that on July 7, 1925, the Patent Office issued patent number

1,544,973 to Ghadiali for a gadget for projecting colored lights. This does not mean that the Patent Office was remotely concerned with the use to which the patentee would put his device. So far as the patent officials were concerned, it was a matter of indifference whether the patented article was used to spot-light a burlesque queen on the stage or to throw pretty colored lights on a shop-window display.

But before Ghadiali had brought his suit, Ernest was advertising—in 1936—that his company was acting as "National Distributor" for another "color ray" concern, that of Karl von Schilling, whose device was dubbed "Vita Chrome (Life Colors)." The von Schilling machine was said to be "Released by National Clinic for Color Ray Research" and to have been "Approved by the National Association of Color Ray Scientists." If there is, or ever was, such a "national clinic" or "national association," their colored lights must have been hidden under a bushel, for we have been unable to find any scientists, either in medicine or physics, who have ever heard of them. By December 1936 Mr. Ernest appears to have severed connections with von Schilling, and from then on seems to have put out his own colored-lights devices, the chief of which Ghadiali claims is an infringement on his own machine. If one is in the hocus-pocus business, why split the swag?

As previously stated, the Ernest devices are named, respectively, "Chromaray" and "Trioray." The former seems to be the one that copies Ghadiali's. It resembles essentially the "spot-light" used in theatres and dance halls to project colored lights on the stage or the dance-floor. The source of light is an electric bulb. The "Trioray" looks like three hand mirrors having metal frames with green and blue lenses, respectively, in the place of mirrors. These are used where electric current is not available, and merely focus the sun's rays through the blue or green lens on to the patient—or victim.

According to the Chromaray advertising, this device has been "Successfully Used for the Treatment of" a list of thirty pathological conditions ranging alphabetically from Accidents and Appendicitis through Cancer, Cataract, Diabetes, Heart Disorders, High Blood Pressure, Low Blood Pressure, Pneumonia, Rupture, Sinus Trouble and Sleeping Sickness to Tuberculosis and Venereal Disease. Lack of space doubtless was all that prevented a completion of the alphabetical list, for of course the Chromaray would be equally efficacious in the treatment of such conditions as Worms, Xerophthalmia, Yaws and Zymotic Zoophobia.

From the Chromaray advertising one learns that red light will "energize" the liver, yellow will move the bowels, orange will supply any need of calcium and green will kill germs and take the place of chlorine. In short, to quote from the ballyhoo booklet on Chromaray: "Color Therapy is 'chromochemical affinization,'" a statement that ranks with some of the jingles in "Alice in Wonderland" in clarity. The theory of Chromaray, is that "Disease is a disturbance of Color balance, due either to the lack of Color in the body or the inability of the organs to absorb or assimilate the color element."

Among the "clinical reports" that appear in the Chromaray booklet is this gem:

"Mr. E. of Vineland, New Jersey, was cured of a terrible case of rheumatic ankylosis of the shoulder by thermolune baths [whatever they are!] and some massage in two or three weeks. Red glass was used over the part."

The incidental mention of "some massage" is quite in character. One might conceive such a report as:

"Little Jimmie X. was cured of a terrible case of diphtheria by the use of pink and blue lights and some antitoxin."

The Chromaray booklet also suggests that blue glass should be used when there are "very acute pains" in "cases of inflammable [sic!] rheumatism." The old idea of spontaneous combustion will not down.

Summing up its thesis, the Ernest Distributing Company delivers this *ipse dixit*:

"The earth has arrived at a Cosmic Cycle of Color Expression."

And thus once again does the unintelligible make its irresistible appeal to the unintelligent.

1. A reprint of an article on Dinshah P. Ghadiali will be sent on receipt of a stamped, addressed envelop.

Correspondence

THE ROLE OF THE ADRENALS IN HYPERTENSION

To the Editor:—In THE JOURNAL, August 6, page 556, appeared a communication from W. B. Cannon concerning an article by Rogoff and Marcus entitled "The Supposed Role of the Adrenals in Hypertension," which was published in THE JOURNAL, June 25. Dr. Cannon has published articles with similar content and manifesting a similar personal attitude on previous occasions (e. g. *Eudokrinologic* 6:24 [Jan.] 1930; *Pharos of A. O. A.*, May 1938).

Dr. Cannon has challenged our statements on which we base argument for serious deprecation of certain risky clinical procedures that can be justified by his so-called emergency theory. He objects to our criticism of the suggestion admittedly made by him (*Am. J. Physiol.* 27:64, 1911) "that hypertension might be dependent on adrenal secretion and that adrenal secretion might be continuously stimulated by circulating epinephrine." Furthermore, he is evidently concerned because we did not refer to certain of his articles. These would only constitute "emphasis on minor points—points having little meaning in relation to the main difference which is at issue" (cf. A. O. A. lecture), and I agree with the statement in his lecture that "value may follow from a polemic if the discussion is kept on a factual level."

Notwithstanding Dr. Cannon's suggestion that I am not cognizant of the literature concerning "chemical mediation of nerve impulses," I am sufficiently familiar with it to recognize much of what may be called clothing old ideas in new terms. Reliability of some of the methods of investigation may be questioned. Existence of chemical mediators that are recognized by acceleration of a denervated heart which has been found to be not completely denervated (Brouha, L. A.: *Science* 83: [Feb. 28] 6, 1936; Cannon, W. B.; Lewis, J. T., and Britton, S. W.: *Am. J. Physiol.* 77:326 [July] 1926) may be considered more or less hypothetical, especially since this nonspecific test object is equally good as a reagent for epinephrine and for accelerator substances from the thyroid, the liver and elsewhere! Nor does this subject have more than "little meaning in relation to the main difference which is at issue." Furthermore, his point that adrenal secretion does not play a role in the maintenance of normal blood pressure also has little meaning in relation to the main difference which is at issue. I would not suppose that Dr. Cannon could believe otherwise, for he contends that there is no adrenal secretion under conditions of normal quiet existence, when a normal blood pressure is nevertheless maintained. That epinephrine secretion from the adrenals is not essential for maintenance of normal blood pressure was demonstrated by Stewart and Rogoff (*J. Pharmacol. & Exper. Therap.* 10:1 [July] 1917; *Am. J. Physiol.* 48:397 [May] 1919) and by Rogoff and Dominguez (*J. Metabolic Research* 6:141, 1924; *Am. J. Physiol.* 83:84 [Dec.] 1927). The point under discussion is concerned with pathologic, not normal, blood pressure.

Rogoff and Marcus quoted from Dr. Cannon's published articles. The quotations represent fundamental premises on which the so-called emergency theory rests. These premises are a basis for the clinical practice of intervention at the adrenals as a means of treatment for diabetes and for hypertension, a practice which involves grave risk to human life and health. We published quantitative evidence that Dr. Cannon's statements, as quoted by us, are not tenable in the light of experimental investigation. Regarding the supposed "autogenous continuance of adrenal secretion," Dr. Cannon (*Am. J. Physiol.* 27:64 1911) stated "Thus also the persistence of the emotional state after the exciting object has disappeared can be explained." Only a few months ago (A. O. A. lecture) he stated "Actual records show that one minute of excitement may have bodily

effects lasting for fifteen-twenty minutes if the adrenals are present and only brief effects if the glands are absent. Actual records show that the production of adrenine in amounts which can have remote influence in the organism is unmistakable." If Dr. Cannon no longer maintains the conclusions which we have quoted from his articles, and if he will refer me to any published withdrawal, I will readily admit error. If these fundamental concepts, deduced from his experimental work, are now denied, on what support does the validity of the emergency theory rest?

In a personal communication to Dr. Cannon, Nov. 11, 1929, under similar circumstances, I stated "I sincerely regret that we have not been able to come to some closer agreement in the matter under discussion. My only interest in the disagreement that exists between us is a conscientious desire to reach a satisfactory scientific explanation of the role of the adrenals. To this end I have often hoped that in some way it might become possible for us to arrive at some premise in our work where we could, perhaps, find it possible to cooperate and strengthen each other's position in the interest of scientific progress." Such a premise may, indeed, now exist since Dr. Cannon apparently no longer believes in the validity of his statements which we quoted. J. M. ROGOFF, M.D., University of Chicago, Chicago.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

MODE OF DEATH FROM PNEUMONIA

To the Editor:—What work has been done and what conclusions have been drawn as to the fundamental cause of death in lobar pneumonia? Is it respiratory or cardiac failure?

L. T. BROWNING, M.D., Kankakee, Ill.

ANSWER.—With the advance of knowledge some old questions, unless they are rephrased, lose their point. In death from lobar pneumonia, more fundamental problems are involved than whether respiration or cardiac action fails first. Death usually occurs in medical shock or in pulmonary edema. Both conditions are often associated with bacteremia. The mechanism of death from bacteremia is still not understood. Bacteria in the blood may produce their effect by changes in the nervous system or other tissues either by exhausting them, by depleting stores of essential body ingredients such as hormones or vitamins, or as the result of changes due to toxic substances from the bacteria, exotoxins or endotoxins.

Pulmonary edema may be due to an extensive lesion which obstructs the lesser circulation or to edema-producing substances coming from the infecting organisms. Medical shock may be due to dehydration resulting from either pulmonary edema or evaporation from the lungs and skin due to the fever. The mass against which the heart may contract is reduced because of the smaller blood volume, so that the heart may ultimately fail. Anoxia is aggravated by poor circulation; the heart is not pumping adequately for the reason just stated. When there is so-called cardiac failure, oxygen and infusions of dextrose and saline solution are more useful than digitalis or other heart stimulants. Direct stimulation of the respiration or the heart is not required.

MAXIMOW'S TISSUE STAIN

To the Editor:—What is the technic of the Maximow tissue stain?

M.D., Massachusetts.

ANSWER.—The stain referred to is probably the hematoxylin-eosin-azure II stain (Maximow). The tissues must be fixed in Zenker formaldehyde solution. Sections to be stained are mounted on slides, the paraffin or celloidin is removed from the sections before staining, then the slides are passed through compound solution of iodine diluted 1:3 with distilled water and 5 per cent thiosulfate solution washed in three changes of distilled water. (a) From the distilled water the slides are trans-

ferred to weak Delafield's hematoxylin overnight, 1 to 2 drops of the stock solution in 100 cc. of distilled water being used (the weak solution must be fresh every time). Only the chromatin and nuclear membranes should stain faintly. (b) The slides are placed in distilled water all day to remove excess stain from the connective tissue. (c) The counterstain is eosin-azure II solution with 5 cc. of eosin solution, 40 cc. of distilled water and 7 cc. of azure II solution. (This solution is made just before use, each part being added in the order given and can be used only once.) The stain is applied overnight. More or less eosin or azure II may be used according to the quality of stain desired. The stock solutions are eosin 0.1 Gm. in 100 cc. of distilled water and azure II 0.1 Gm. in 100 cc. of distilled water. (d) The slides are differentiated in 95 per cent alcohol, each slide being looked at frequently under the microscope, until the nuclei are deep blue and the collagenous fibers are pink. They are dehydrated quickly in two changes of absolute alcohol and cleared in two changes of xylene fifteen minutes each and mounted in Damar. Some blue is removed in the dehydrating alcohols, so the slides should be started through them before differentiation is complete. When differentiated properly the nuclei should be deep blue, the cytoplasm varying shades of blue, the smooth muscle pale lavender, the connective tissue fibers pale pink and the red blood cells orange red or pale green. Delafield's hematoxylin should age four months before use and should not be used after it is eight months old.

TUBERCULOSIS IN MEAT PACKING INDUSTRY

To the Editor:—I would appreciate information as to the incidence of tuberculosis among persons working in meat packing plants where they frequently enter the refrigerator.

J. B. WILETS, M.D., Milwaukee.

ANSWER.—A careful search has failed to reveal statistics concerning the incidence of tuberculosis among persons working in meat packing plants where they frequently enter the refrigerator.

The United States Department of Agriculture, Bureau of Animal Industry, Washington, D. C., has no available information on this subject.

Physicians connected with large meat packing plants in Chicago have stated that the incidence of tuberculosis among meat packing workers and those employed in and out of refrigerators is not higher than in the employees of the packing plants in general or higher than the incidence of tuberculosis in workers at large.

"DOUBLE HEARING"

To the Editor:—A woman of 68, definitely not a neurotic, complains that following an explosion in a telephone receiver in March 1932 she became deaf in the right ear for a day. Her hearing returned, but she experienced an effect of "double hearing." Every sound repeats itself like an echo. The echo effect is close to the original sound; for example, the word "father" sounds like "fatherther." Her blood pressure is 190 systolic, 100 diastolic, and a whispered voice is heard only at five feet on the right side. Other ear, nose and throat examinations, including caloric tests, are normal. The patient was examined by a competent neurologist, who does not find any other symptoms.

S. H. PORTNOY, M.D., Cincinnati.

ANSWER.—"Double hearing" may be of several varieties. One type is known as diplacusis dysharmonica. In this variety the patient complains of hearing the same sound but with a different pitch in each ear. The pitch in the affected ear is usually higher but may be lower than in the normal ear. Another type of so-called double hearing has been described by Kayser as diplacusis echoica. Sound heard in the affected ear is repeated more or less as an echo. These forms of "double hearing" may be due to disease in the middle ear or in the cochlea. There are a number of theories regarding the mechanism, but no really satisfactory answer is available.

A number of observers accept the Helmholtz resonator theory of hearing, which assumes that separate tones are analyzed not in the eighth nerve and its central pathways but in the cochlea, where individual or groups of hair cells are stimulated by only certain tones, depending on the location of these cells in the cochlea. In general, high tones affect the hair cells near the basal turn of the cochlea; low tones affect those near the apex. An injury to the basilar membrane or an exudate weighing it down will cause the latter to vibrate abnormally and hence cause the particular hair cells resting on this membrane to transmit a faulty message to the brain. Those subscribing to this theory feel that diplacusis binauralis dysharmonica and echoica are due to lesions in the cochlea and not in the middle ear. There are others, however, who feel that the pathologic condition may be in the middle ear.

This patient should have a complete examination of the hearing to determine why the whispered voice is only heard at five feet

on the affected side. Should the examination reveal a conduction form of deafness, treatment may be of considerable avail. From the few cases described in the literature it would appear that a fair number of these complaints seem to cure themselves spontaneously by the passage of time. It is quite possible that the acoustic insult described was responsible for the disturbances of which the patient complains.

References:

- Poltzer, Adam: Textbook of the Diseases of the Ear, ed. 6, Philadelphia, Lea & Febiger, 1926.
Kayser (Berlin Congress 1890, quoted by Politzer).
Proetz, Arthur: Diplacusis Binauralis Dysharmonica, *Ann. Oto., Rhin. & Laryng.* 46: 119 (March) 1937.
Shambaugh, G. E., Jr.: Syndrome of Diplacusis and Nerve Deafness for Low Tones, *Arch. Otolaryng.* 21: 694 (June) 1935.

EFFECT OF SULFUR CHLORIDES ON EYES

To the Editor:—What is the effect on the eyes, especially the macular bundle with a reaction similar to toxic amblyopia, from breathing fumes from sulfur monochloride or chloride? This is supposed to be oxidized on contact with air.

U. D. SEIDEL, M.D., Akron, Ohio.

ANSWER.—Sulfur chloride on contact with air is probably not oxidized but hydrolyzed to hydrochloric acid and possibly hydrogen sulfide or sulfur dioxide. There is no evidence that sulfur chloride or its hydrolytic products possess any special capacity to attack the macular bundle or to lead to toxic amblyopia, but sulfur dioxide and hydrogen sulfide irritate the mucous membranes including the conjunctiva. In fact, some writers indicate that sulfur chloride itself is nontoxic. Hamilton (Industrial Poisons in the United States, New York, Macmillan Company, 1929) states that sulfur monochloride "is apparently nontoxic" and quotes Lchmann as having noted that it is "practically harmless." However Kober and Hayhurst (Industrial Health, Philadelphia, P. Blakiston's Son and Company, 1924) state that the decomposition products of sulfur chloride are injurious. It is well known that hydrogen sulfide is a toxic chemical. In some industries, sulfur chloride is used in conjunction with carbon disulfide, in which case the latter substance is to be regarded as the more dangerous. Carbon disulfide has produced amblyopia, retinitis and bulbar neuritis but so far as known not as the exclusive manifestation of its action. More recently, sulfur chloride has been described as possessing damaging properties in its own right—jaundice, neuritis, myelitis and profound weight losses are said to be characteristic.

Adler, in the Proceedings of the Fifth International Medical Congress on Occupational Diseases, in 1928, reported clinical and laboratory work related to the action of sulfur chlorides. Earlier, Adler-Herzmark reported in International Labour Office studies (Industries Hygiene, 1926, No. 10, p. 76) poisoning by sulfur monochloride in the absence of carbon disulfide, in which the patient presented jaundice, great loss of weight, and paralysis of the forearms, legs, bladder and rectum. After a short period the major disturbances disappeared, leaving some atrophy of the leg muscles, associated with paralysis of these extremities. In general, it is believed that sulfur chloride or its hydrolytic products might induce injury to the eye, but apparently only in case there coexisted other and more characteristic evidences of injury from this source.

HYSTERECTOMY AND INCIDENCE OF CANCER

To the Editor:—Please let me have some information on (1) the incidence of thyroid disease after hysterectomy previous to the menopause; (2) the incidence of carcinoma of the cervix in patients following supra-cervical hysterectomy as compared with women not operated on; (3) the incidence of carcinoma of the cervix in hysterectomized patients before and after the menopause.

M.D., Ohio.

ANSWER.—1. As far as is known there are no statistics about the incidence of thyroid disease after hysterectomy previous to the menopause.

2. In a series of 7,244 subtotal hysterectomies collected from the literature by von Graff (*Am. J. Obst. & Gynec.* 28:18 [July] 1934) carcinoma was subsequently found in the cervical stump in forty-five instances, an incidence of 0.62 per cent. Likewise in the literature von Graff found that there were 176 cases of cancer of the cervical stump among 4,269 cases of cervical cancer, a frequency of 4.1 per cent of all cervical cancers. Von Graff says: "Comparing the 0.6 per cent possibility of cancer after subtotal hysterectomy with the actual frequency of 4 per cent of stump cancer, every unprejudiced observer must admit that the danger of cancerous degeneration, present at the time of operation or developed later, is more than six and a half times as great as ordinarily reckoned. In addition it is fair to presume that many instances exist which have not come to our knowledge. . . . The real frequency of stump cancers may amount to several times the number revealed in this paper."

It is essential to determine whether cancer in the stump of the cervix was present at the time of the supracervical hysterectomy or appeared later. Von Graff assumed that cancers found within one year after a hysterectomy were present at the time of the operation. In a series of 581 cancers of the cervical stump he found that 137, or 23.5 per cent, were present at the time of the supracervical hysterectomy and that only 76.5 per cent developed subsequently.

3. The age of patients with cancer of the cervical stump has no significance. This form of cancer occurs at any age from 20 to over 70 years. Whereas the large majority of the stump cancers occurred in women between 36 and 60 years of age, 11.3 per cent of von Graff's series were found in women between 20 and 35 years of age. Hence the possibility of this form of malignancy must be taken into account regardless of the youth of the patient. Approximately one third of the patients in von Graff's series were past 50 years of age.

HYPERTENSION AND ACUTE ANEMIA

To the Editor:—A man aged 56, once a nationally famous athlete, complained of frequent dizziness, slurring of speech, weakness in the legs (especially the left), nocturia and difficulty in controlling urination. Thirteen months ago physical examination revealed a slight deviation of the tongue to the right, a moderately hypertrophied heart, a blood pressure reading of 280/160, shuffling gait, and no appreciable objective loss of strength in the extremities. Rectal examination showed a slightly hypertrophied prostate. The blood vessels were slightly arteriosclerotic. Urinalysis showed granular casts, albumin 2 plus, specific gravity 1.011. The Wassermann reaction was negative. On a diagnosis of chronic nephritis with malignant hypertension, the patient was treated with phenobarbital, glyceryl trinitrate, theobromine with sodium acetate, digitalis, fluids freely, low salt diet and restricted activity. He improved considerably, the blood pressure descending to 160/120 at times, with frequent fluctuations to a maximum of 200 mm. systolic or over. Urinalysis was negative at frequent intervals and nocturia was less frequent. Three days ago the patient complained of an increase in the severity of his symptoms. The blood pressure was 280/160. He was hospitalized and on the next morning the blood pressure reading was estimated to be about 320/160, as it seemed to register about 20 mm. higher than the 300 mm. maximum possible on the sphygmomanometer. A venesection of 500 cc. of blood was done with a drop in pressure to 248/140. The patient felt better. He was placed on phenobarbital, glyceryl trinitrate and digitalis. About five hours after the venesection the patient suddenly became irrational, tried to get out of bed, had convulsive movements of the left extremities and then lapsed into a deep coma with frothing at the mouth. The blood pressure taken at this time was over 300 mm. systolic. He remained in coma until his death four hours later. My impression is that he died of apoplexy. Please discuss (1) the maximum heights of blood pressure ever recorded and prognosis at various levels, (2) changes of blood pressure from venesection and (3) diagnosis and treatment of such a case.

M.D., Hawaii.

ANSWER.—Probably the patient had had a minor cerebral accident when he was first seen, but the terminal episodes resemble acute uremia rather than cerebral apoplexy. The renal elements of his disease seem to have been neglected both diagnostically and therapeutically. The query does not state under what conditions of water balance the urinary specific gravity of 1.011 was obtained; if the specimen was voided under conditions of relative dehydration, as in a renal concentration test, such low specific gravity is of the greatest significance and implies grave and alarming depletion of the renal functional reserve. No mention is made of the blood picture; it may be assumed, however, that a relatively severe grade of anemia existed with such extensive renal damage. Transfusion of blood rather than venesection might have prolonged his life temporarily (but only briefly), for the extensive renal arteriolar constriction and anemia are the major factors in aggravating renal failure. The kidneys require a liberal supply of oxygen; anything which diminishes the oxygen available to the renal parenchyma may precipitate acute renal failure and uremia when the renal reserve is grossly depleted. No mention is made of evidences of cardiac exhaustion despite the tremendously high diastolic tension.

Levels of systolic tension from 300 to 400 mm. of mercury are unusual but not extremely rare. Without exhaustive search it is impossible to state exactly the maximum arterial tension ever recorded. The diastolic tension is the more significant of the two, as regards both the height of the tension and its variability. In severe acute arterial spastic states (as in eclampsia) the diastolic tension has been observed above 200 mm. of mercury. There is no satisfactory correlation between the level of the arterial tension and the prognosis in individual instances; many factors are involved. The fixedness of the diastolic tension, for example, is more significant than the maximum level, for it reveals the extent of irreparable arteriosclerotic degeneration. Factors such as age, the duration

of the hypertensive arterial disease, the rate of its progression, the cardiac and renal functional reserves, the nature of the provoking etiologic factors and the inherent vulnerability of the patient (often partially revealed by the family history) must all be considered (Stieglitz, E. J.: Arterial Hypertension, *Arch. Int. Med.* 46:227 [Aug.] 1930).

Venesection, with the removal of from 200 to 500 cc. of blood, usually causes a temporary reduction of the arterial tension but is of little therapeutic value except in acute cardiac failure with increased venous pressure. In such instances the temporary relief gives the heart a short "breathing spell" and may turn the tide toward recovery of compensation. As the transient reduction of arterial tension following phlebotomy is usually followed by a further rise in the tension, the procedure in cases of cerebral accident is associated with definite risk.

Adequate diagnosis must include not merely the name of a disease but an understanding of its complex and multiple causation, an evaluation of the functional capacity of the injured structures (here the arterioles, kidneys and heart) and search for complicating disease processes. In the present instance renal function studies and blood examinations were needed. Evaluation of the renal functional capacity serves not only to clarify diagnosis but also to reveal the benefit (or lack of benefit) of therapeutic measures. The anemia of nephritis and/or severe hypertensive arterial disease is a most significant factor in the self perpetuation and progression of the disease.

Apparently nothing was done therapeutically for the nephritic element. There is no specific therapy for nephritis, but realization of the renal mechanisms for the secretion of urine points out two vital therapeutic indications: (1) correction of any anemia so that the kidneys may have as good a blood supply as possible (this frequently will also reduce the hypertension) and (2) a large fluid intake. The intake of water should be pushed almost to the limit of cardiac endurance, for the fundamental functional failure in nephritis is the inability of the renal secreting mechanism to concentrate the urine. Therefore, in order that the toxic solutes and metabolic debris may be adequately eliminated, it is imperative that a large volume of urine be secreted. From 3 to 5 liters of fluid daily is not excessive for uremic or preuremic patients, if it is consumed in small quantities at frequent intervals.

PROVOCATIVE PHENOMENON IN SYPHILIS

To the Editor:—What dose of arsphenamine should be used for a provocative test for syphilis? Authorities do not seem to agree. What is the time between the giving of the drug and the taking of blood for the Wassermann test?

ROY A. ZINK, M.D., Tulsa, Okla.

ANSWER.—Studies of the provocative phenomenon in syphilis so far carried out are inconclusive on three scores: (a) the dosage of the arsenical to be employed, (b) the proper time interval between tests after treatment and (c) the use up to this time of a qualitative rather than a quantitative serologic technic. Such information as is available indicates that in all patients with early syphilis and in the majority of those with late syphilis, the first injection of a therapeutic dose of an arsphenamine (e. g., arsphenamine 0.3-0.4 Gm., neoarsphenamine 0.45-0.9 Gm., mapharsen 40-60 mg. and so on) is followed within five to seven days by a quantitative rise in reagin titer, which falls to or below its original level by the fourteenth day after treatment.

The provocative test is of no value whatever as a determinant of "cure" in a patient who is seronegative following treatment, since the provocative phenomenon often fails to appear in individuals whose subsequent course includes definite progression or relapse.

Almost the only circumstance in which the provocative test is of value is for the confirmation of the diagnosis in individuals previously untreated, in whom the presence of syphilitic infection is suggested by a low titer reagin content of the blood; i. e., those in whom doubtful or weakly positive serologic tests are obtained. In such persons the administration of a therapeutic dose of an arsphenamine is often followed by a quantitatively measurable increase in reagin titer, and if such an increase occurs the diagnosis of syphilis may be regarded as confirmed.

The suggested procedure is: (a) a preliminary serologic test on a quantitative basis, (b) the intravenous administration of a therapeutic dose of any of the arsphenamines, (c) repetition of the quantitatively titrated serologic test at forty-eight hour intervals for a minimum of from ten to fourteen days.

No reliance should be placed on the result of the tests unless the laboratory is prepared to furnish quantitative titrations.

MELANCHOLIA AND INCREASED LIBIDO

To the Editor:—A man aged 50 has complained for the past year of symptoms of involuntional melancholia, consisting of periods of extreme depression, crying spells, discouragement and even a desire for death. At the same time the libido has become increased, although physically the patient is unable to meet the demands of this excessive sexual desire. He shows a decided preference for the company of young people, both male and female, which is unusual for him. He imagines himself in love with a young girl employee, although he realizes that this is probably a manifestation of his increased libido. His insight into his condition is remarkably good. He shows no symptoms of any major psychosis. Physical examination and blood examination are negative. During the past year he has received theelin in oil, bromides and at one time benzedrine sulfate. The depression seemed to clear with the benzedrine sulfate temporarily but recently he has been getting worse. He is happily married, loves his wife and yet feels that his condition may break up his home. Recently he has contemplated suicide on several occasions. Will you please outline the best plan for the relief of his condition? Would local medications to the verumontanum have any effect in decreasing his sexual desire? If this is purely an involuntional state, which endocrines would you advise administering? Would ligation of the vas have any beneficial effect?

M.D., New Hampshire.

ANSWER.—This patient is evidently going through a period of depression and would perhaps best be treated away from his present environment in an institution where proper psychotherapeutic and medical methods would be employed. In addition, there should be adequate safeguards against any suicidal attempts or gestures. Such patients require planned psychotherapy, adequate exercises and occupational therapy, tubbing, and occasional small doses of barbitol to ease the symptoms of depression. Ligation of the vas would not have any beneficial effect but, on the contrary, might even increase the causes for the patient's depression. Local medications to the verumontanum would only fixate this depression to the sexual sphere and thereby perhaps overemphasize the sexual component of the patient's illness.

"DENICOTINIZED" CIGARS AND CIGARETS

To the Editor:—I have had to give up tobacco but have heard of Carl Henry cigars and cigarettes, which are supposed to have had most of the nicotine removed. Can you inform me as to the facts?

R. W. FORD, M.D., Otego, N. Y.

ANSWER.—Although denicotinization is a laboratory possibility, no completely denicotinized product is yet commercially available. According to their own advertisements, Carl Henry cigars and cigarettes contain from 0.6 to 1 per cent of nicotine. The average popular brands of cigarettes on the market for which no special claims of denicotinization are made contain on the average 2 per cent and cigars about 1.7 per cent. Accordingly, three Carl Henry cigars or cigarettes contain about as much nicotine as do two ordinary ones. Any reliance placed on the processing leading to the consumption of more of the so-called 'denicotinized' products may therefore lead to a greater nicotine intake than if untreated brands were used.

References:

- Bailey, E. M.: Bull. 295, Connecticut Agricultural Experiment Station, May 1928.
Bogen, Emil: Irritant Factors in Tobacco Smoke, *California & West. Med.* 45: 342 (Oct.) 1936.

QUININE IN LATE PREGNANCY

To the Editor:—What is the current opinion as to the use of quinine in small doses for several weeks prior to the onset of labor for the purpose of shortening the duration and decreasing the pain? Would there be any harm to the mother or the child, aside from the occasional idiosyncrasy to quinine, in administering the dihydrochloride in doses of 1 grain (0.065 Gm.) three times a day for about four weeks before the onset of labor?

MICHAEL BALLIN, M.D., Chicago.

ANSWER.—There has been a general impression that small doses of quinine given to a patient during the last month or so of pregnancy will result in a shorter and less painful labor. This practice has found little vogue in this country. Recently Smith reported a small group of cases in which the patients received 0.1 Gm. (1½ grains) of quinine dihydrochloride three times a day during the last three weeks of their gestation with favorable results.

Pharmacologically, quinine is a poor and ineffective oxytocic drug. It may, however, act as a general tonic, thereby having some influence on the uterus. There are a number of undesirable effects from the use of this drug, in addition to the idiosyncrasy on the part of the patient which has been mentioned. Occasionally a baby succumbs in utero during a quinine induction of labor, even though only small doses of the drug were used and at autopsy nothing is found to account for the fetal death. Furthermore, a recent publication traced the origin of nerve deafness in children to the administration

of quinine to their mothers. These undesirable effects and the lack of clearcut proof that the administration of small doses of quinine late in pregnancy has any favorable results on the labor make it inadvisable to administer the drug to patients in a routine manner.

References:

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Adair, Fred L., and Davis, M. Edward: A Study of Human Uterine Motility, *Am. J. Obst. & Gynec.* 27: 383 (March) 1934.
Davis, M. Edward: The Use and Abuse of Ergot and Pituitary, *Taz Journal*, Nov. 13, 1937, p. 1631.

GONORRHEA AND ENLARGED PROSTATE IN ELDERLY MAN

To the Editor:—A man aged 63 has an enlarged middle lobe of the prostate with a 4 ounce urinary retention. October 22, 1937, he contracted an acute gonorrheal infection and a short time later a cystitis. There were no other complications. The urethral discharge cleared up in about a month but both glasses remain cloudy and an examination of a centrifuged specimen of the urine shows pus and gram-negative intracellular diplococci, which I assume are from the bladder. He has no frequency and gets up only once at night. I have given him various urinary antiseptics, including sulfanilamide in large doses. I am now giving him foreign protein injections intramuscularly. I have also massaged his prostate, which is normal in size. Have you any suggestions?

M.D., Connecticut.

ANSWER.—The administration of urinary antiseptics, including sulfanilamide, will probably not benefit this patient much, nor will foreign protein injections help much. These statements are based on the fact that the patient is 63 years of age, has a large middle lobe of the prostate, and 4 ounces of residual urine and pus in the urine.

If the organisms are gonococci and the patient has a gonococcal infection of the bladder, the persistence of the gonococci in the urine is due no doubt to the fact that the patient has an obstruction at the bladder neck with resulting residual urine. A complete urologic study is desirable, including routine roentgen study of the entire tract to rule out the possibility of stone. A set of intravenous pyelograms should be made in order that one may have an understanding of the pathologic condition of the upper urinary tract. Finally, careful study of the renal function should be carried out.

After these examinations have been made and if there are no contraindications, a transurethral resection of the prostate would be advisable.

SACCHARIN IN DIABETES

To the Editor:—Please give the indications for the use of saccharin in diabetes.

M.D., Louisiana.

ANSWER.—Properly speaking, there are no indications for the use of saccharin in the treatment of diabetes, for this substance has no inherent therapeutic properties. However, it is commonly used to impart sweetness to foodstuffs in place of the sugars. In this way it may be of therapeutic value indirectly by rendering a low carbohydrate diet more palatable and removing the temptation to "cheat" on the diet. The sweet taste of saccharin is not strictly comparable to that of dextrose or sucrose. Even a slight excess of saccharin may introduce an objectionable bitter after-taste. It should therefore be used in moderation, with the purpose of counterbalancing excessive sourness or bitterness in foods rather than of making them really sweet.

REMOVAL OF TOBACCO STAINS FROM TEETH AND SKIN

To the Editor:—What is the best procedure for removing tobacco stains from the teeth and cigarette stains from the fingers? Several patients have inquired and I have no satisfactory answer.

M.D., New York.

ANSWER.—Dentists remove tobacco stains from the teeth by scouring them with pumice. Some of them wet the powder with a small amount of hydrogen peroxide. Tobacco stains on the skin can be removed by rubbing with acetone.

REPEATED ORGASM

To the Editor:—A patient of mine relates the following sexual episode, and I am interested in determining its veracity in your opinion: He states that during intercourse he has an ejaculation and then is able to maintain an erection without the appearance of flaccidity. About ten or fifteen minutes after the first ejaculation active intercourse is repeated, with another ejaculation. Is this physiologically normal?

M.D., New York.

ANSWER.—Yes.

Medical Examinations and Licensure

COMING EXAMINATIONS

STATE AND TERRITORIAL BOARDS

ALABAMA: Montgomery, Jan. 3-5 and June 20-22. Sec., Dr. J. N. Baker, 517 Dexter Ave., Montgomery.

ARKANSAS: *Medical (Regular).* Little Rock, Nov. 3-4. Sec., State Medical Board of the Arkansas Medical Society, Dr. L. J. Kosminsky, Texarkana. *Medical (Eclectic).* Little Rock, Nov. 3. Sec., Dr. Clarence H. Young, 1415 Main St., Little Rock. *Basic Science.* Little Rock, Nov. 7. Sec., Mr. Louis E. Gebauer, 701 Main St., Little Rock.

CALIFORNIA: *Written examination.* Sacramento, Oct. 17-20. *Reciprocity.* Los Angeles, Nov. 16. Sec., Dr. Charles B. Pinkham, 420 State Office Bldg., Sacramento.

CONNECTICUT: *Medical (Regular).* Hartford, Nov. 8-9. Sec., Dr. Thomas P. Muddock, 147 W. Main St., Meriden. *Medical (Homoeopathic).* Derby, Nov. 8-9. Sec., Dr. Joseph H. Evans, 1488 Chapel St., New Haven.

DELAWARE: Dover, July 11-13. Sec., Medical Council of Delaware. Dr. Joseph S. McDaniel, 229 S. State St., Dover.

DISTRICT OF COLUMBIA: *Basic Science.* Washington, Dec. 26-27. *Medical.* Washington, Jan. 9-10. Sec., Commission on Licensure, Dr. George C. Ruhland, 203 District Bldg., Washington.

FLORIDA: Jacksonville, Nov. 14-15. Sec., Dr. William M. Rowlett, Box 786, Tampa.

ILLINOIS: Chicago, Oct. 18-20. Superintendent of Registration, Department of Registration and Education, Mr. Homer J. Byrd, Springfield.

INDIANA: Indianapolis, June 20-22. Sec., Board of Medical Registration and Examination, Dr. J. W. Bowers, 301 State House, Indianapolis.

KANSAS: Topeka, Dec. 13-14. Sec., Board of Medical Registration and Examination, Dr. J. F. Hassig, 905 North 7th St., Kansas City.

KENTUCKY: Louisville, Dec. 6-8. Sec., State Board of Health, Dr. A. T. McCormack, 620 S. Third St., Louisville.

MAINE: Portland, Nov. 8-9. Sec., Board of Registration of Medicine, Dr. Adam P. Leighton, 192 State St., Portland.

MARYLAND: *Medical (Regular).* Baltimore, Dec. 13-16. Sec., Dr. John T. O'Mara, 1215 Cathedral St., Baltimore. *Medical (Homoeopathic).* Baltimore, Dec. 13-14. Sec., Dr. John A. Evans, 612 W. 40th St., Baltimore.

MASSACHUSETTS: Boston, Nov. 8-10. Sec., Board of Registration in Medicine, Dr. Stephen Rushmore, 413 F. State House, Boston.

MINNESOTA: Minneapolis, Oct. 18-20. Sec., Dr. Julian F. Du Bois, 350 St. Peter St., St. Paul.

MISSISSIPPI: *Reciprocity.* Jackson, December. Asst. Sec., State Board of Health, Dr. R. N. Whitfield, Jackson.

MISSOURI: Kansas City, Oct. 18-20. State Health Commissioner, Dr. Harry F. Parker, State Capitol Bldg., Jefferson City.

NEBRASKA: Lincoln, Nov. 25-26. Dir., Bureau of Examining Boards, Mrs. Clark Perkins, State House, Lincoln.

NEVADA: Carson City, Nov. 7-9. Sec., Dr. John E. Worden, Capitol Bldg., Carson City.

NEW JERSEY: Trenton, Oct. 18-19. Sec., Dr. James J. McGuire, 28 W. State St., Trenton.

NORTH CAROLINA: *Reciprocity.* Raleigh, December. *Examination.* Raleigh, June 19. Sec., Dr. William D. James, The Hamlet Hospital, Hamlet.

NORTH DAKOTA: Grand Forks, Jan. 3-6. Sec., Dr. G. M. Williamson, 4½ S. Third St., Grand Forks.

OKLAHOMA: *Basic Science.* Oklahoma City, Nov. 30. Sec. of State, Hon. Frank C. Carter, State Capitol Bldg., Oklahoma City. *Medical.* Oklahoma City, Dec. 14. Sec., Dr. James D. Osborn Jr., Frederick.

OREGON: *Basic Science.* Portland, Nov. 19. Sec., State Board of Higher Education, Mr. Charles D. Byrne, University of Oregon, Eugene.

PENNSYLVANIA: Philadelphia, January. Sec., Board of Medical Education and Licensure, Dr. James A. Newpher, 400 Education Bldg., Harrisburg.

SOUTH CAROLINA: Columbia, Nov. 8. Sec., Dr. A. Earle Boozer, 505 Saluda Ave., Columbia.

SOUTH DAKOTA: Pierre, Jan. 17-18. Director of Medical Licensure, Dr. B. A. Dyar, State Board of Health, Pierre.

TEXAS: Houston, Nov. 14-16. Sec., Dr. T. J. Crowe, 918-20 Mercantile Bldg., Dallas.

VERMONT: Burlington, Feb. 14. Sec., Board of Medical Registration, Dr. W. Scott Nay, Underhill.

VIRGINIA: Richmond, Dec. 14-16. Sec., Dr. J. W. Preston, 30½ Franklin Road, Roanoke.

WEST VIRGINIA: Bluefield, Oct. 31-Nov. 2. Sec., Public Health Council, Dr. Arthur E. McClug, State Capitol, Charleston.

WISCONSIN: Madison, Jan. 10-14. Sec., Dr. Henry J. Gramling, 2203 S. Layton Blvd., Milwaukee.

SPECIAL BOARDS

Examinations of Special Boards were published in THE JOURNAL, October 8, page 1401.

Maine July Report

Dr. Adam P. Leighton, secretary, Maine Board of Registration of Medicine, reports the written examination held at Augusta, July 5-6, 1938. The examination covered ten subjects and included 100 questions. An average of 75 per cent was required to pass. Nineteen candidates were examined, eighteen of whom passed and one failed. Seven physicians were licensed by reciprocity. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
Georgetown University School of Medicine.....	(1937)	82, 87	
Johns Hopkins University School of Medicine.....	(1935)	83	
Harvard University Medical School.....	(1932)	79	
Tufts College Medical School.....	(1933)	78, (1937) 80, 85, 85, 86,	
(1938) 85			
Columbia University College of Physicians and Surgeons.....	(1933)	84, (1937) 86	

New York University College of Medicine.....	(1935)	82	
Hahnemann Medical College and Hospital of Philadelphia.....	(1935)	84	
Queen's University Faculty of Medicine.....	(1938)	86	
McGill University Faculty of Medicine.....	(1921) 75.1, (1934)	84	
Université de Lausanne Faculté de Médecine.....	(1933)	80*	

School	FAILED	Year Grad.
Rheinische Friedrich-Wilhelms-Universität Medizinische Fakultät, Bonn.....	(1933)	

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
Georgetown University School of Medicine.....	(1936)	Dist. Colum.	
Johns Hopkins University School of Medicine.....	(1907)	Maryland	
St. Louis University School of Medicine.....	(1930)	Illinois	
Bellevue Hospital Medical College.....	(1885)	Minnesota	
Jefferson Medical College of Philadelphia.....	(1935)	Penna.	
University of Vermont College of Medicine.....	(1936)	Vermont	
Medical College of Virginia.....	(1937)	Virginia	

* License has not been issued.

Colorado July Examination

Dr. Harvey W. Snyder, secretary, Colorado State Board of Medical Examiners, reports the written examination held at Denver, July 6-8, 1938. The examination covered eight subjects and included 163 questions. An average of 75 per cent was required to pass. Fifteen candidates were examined, thirteen of whom passed and two failed. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
Northwestern University Medical School.....	(1937)	81	
University of Illinois College of Medicine.....	(1938)	86	
Julius-Maximilians-Universität Medizinische Fakultät, Würzburg.....	(1922)	76	
Universität Rostock Medizinische Fakultät.....	(1934)	81	
Osteopaths*.....	78.5, 79, 80, 81, 81.3, 81.5, 83,	84, 87	

School	FAILED	Per Cent
Osteopaths*.....	72, 73	

* Examined in medicine and surgery.

Vermont June Report

Dr. W. Scott Nay, secretary, Vermont State Board of Medical Registration, reports the written examination held at Burlington, June 15-17, 1938. The examination covered twelve subjects and included ninety questions. An average of 75 per cent was required to pass. Twenty-one candidates were examined, all of whom passed. Two physicians were licensed by endorsement. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
Georgetown Univ. School of Medicine.....	(1932) 85.2,*	(1934) 88	
Cornell University Medical College.....	(1938)	87.2*	
University of Vermont College of Medicine.....	(1937)	85.1,*	
(1938) 80.1,* 82,* 82.5,* 85.1,* 85.3,* 85.6,* 85.8,* 87.1,* 87.1,* 87.9,* 88,* 88.3,* 88.4,* 88.9,* 89.1,* 89.3,* 91.4*			

School	LICENSED BY ENDORSEMENT	Year Endorsement of
New York University, University and Bellevue Hospital Medical College.....	(1926)	New Jersey
University of Vermont College of Medicine.....	(1937)	N. B. M. Ex.

* License withheld pending completion of internship.

South Dakota July Report

Dr. Park B. Jenkins, secretary, South Dakota State Board of Medical Examiners, reports the written examination held at Rapid City, July 19-20, 1938. The examination covered thirteen subjects and included 100 questions. An average of 75 per cent was required to pass. Seven candidates were examined, all of whom passed. Six physicians were licensed by reciprocity. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
University of Arkansas School of Medicine.....	(1937)	84	
Rush Medical College.....	(1937)	80, 88	
University of Minnesota Medical School.....	(1937) 89,	(1938) 86	
Creighton University School of Medicine.....	(1937)	88	
University of Nebraska College of Medicine.....	(1937)	90	

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
University of Colorado School of Medicine.....	(1935)	Colorado	
State University of Iowa College of Medicine.....	(1925), (1935)	Iowa	
University of Louisville School of Medicine.....	(1934)	Kentucky	
Creighton University School of Medicine.....	(1936)	Iowa	
Marquette University School of Medicine.....	(1934)	Wisconsin	

Book Notices

The Horse and Buggy Doctor. By Arthur E. Hertzler, M.D. Cloth. Price, \$2.75. Pp. 322, with 10 illustrations. New York & London: Harper & Brothers, 1938.

Now and then a book by a physician is selected to be the "book of the month" by those who make these choices. This autobiography by Arthur E. Hertzler is well chosen, for it is so human, so vital, so sensitive, so reasonable and so direct that it captures the interest, if not the complete sympathy, of those who read it. Dr. Hertzler has seen life at first hand. As nearly, apparently, as it can be done he has combined the personality of the old family doctor with the science and knowledge of the modern physician. He has been successful, but not beyond his merit, and he has been happy because he has done the work that he wished to do without considering too much what others thought about him and his work. Although untrained in psychoanalysis, he knows his people and he probably gets results like those achieved by psychoanalysts and psychologists simply because he does know his people. There has seldom been a work published by a physician which will strike a more sympathetic note among doctors, simply because Hertzler speaks freely and with insight. Some of his aphorisms will be quoted for years to come. A few examples may suffice.

Regardless of what the old doctor was able to accomplish in a therapeutic way, the sense of security inspired by the doctor's arrival affected the patients favorably.

The ability of the old type doctor was enhanced because he remained at the patient's bedside until his suffering was relieved, even though it required many hours to achieve that end.

It may be said that one of the most important problems of the family doctor is to determine when or if the patient should consult a specialist and select a reliable one for him.

One need have no compunction in calling certain types of patients "female complainers," for that is just what they are.

Operative treatment is the spectacular part of the doctor's life.

Human nature being what it is, if any one does something that sticks his head above his environment he invites the inevitable brickbat.

In the hospital field, standardization has sought to compel us of the typical prairie states to adopt the ideas of the more wealthy areas. The extravagant architecture naturally has resulted in vastly increased costs of hospital care, which in recent years has so vastly concerned those who have brought it on themselves. They should have thought of that before they started their building program. If one lives in a palace when he is well naturally he feels that he must be sick in one. Those of the common herd who think marble is used only for gravestones do not miss it when they go to a hospital.

To the doctor the human being is primarily an animal actuated by the fundamental urges common to all animals.

Anger as a disturber of health is a less potent factor than fear but as such is often overlooked.

Public service in large measure is able to protect the public from infectious disease whether it wishes it or not. The cure of individual disease is much more difficult to force on the patient. The difficulty, therefore, lies not in the availability of adequate medical service but in the intelligence of the patient to use it. The term intelligence must be given a broad application.

Guinea Pigs and Bugbears. By G. L. Eskew. Cloth. Price, \$1.50. Pp. 269, with 21 illustrations. Chicago: Research Press, 1938.

This book is admittedly promulgated for the purpose of dispelling fears and cautious which the public may have developed as a result of the propaganda of such organizations as Consumers' Research and Consumers' Union. One of the principal contentions of the author is that these organizations are not qualified to give advice, and, so far as that applies to medical information which has appeared to date in some of the publications of those organizations, the reviewer agrees. It must be stated, however, in all fairness that these organizations have probably never wandered any farther from fact than this author does in condemning them. A reprint of a roentgenogram of a pathologic colon is reproduced from a publication by Consumers' Union and compared with an anatomic drawing which the author labels a normal healthy colon. Such colons, as depicted in the roentgenogram, do exist, while the drawing which the author labels a normal healthy colon merely indicates comparative anatomic relationships. He claims that the title of the text "100,000,000 Guinea Pigs" is unjustified because "Everything that can be tested is tested before it is manufactured [sic] and offered to the public. . . . Manufacturers do not wait to observe the effects of their medicines upon human beings. It has already been worked out." One who attempts to act as an authority in these matters should be

fully familiar with the fact that a great many preparations which are placed on the market are not pretested. As a matter of fact this text contains reference to the Elixir of Sulfanilamide episode, but the author dismisses it lightly as follows: "The worst that can be said is that it was an error. The manufacturers admit the error, and have in numerous instances made financial amends, which is the best they can do. . . . The law however should provide. . . ." Thus does one who glorifies manufacturers excuse one of them for an error which caused deaths by the score. The author decries certain misinformation released by consumers' organizations, but some of his own statements are equally misinforming. His subheading for the chapter on Proprietary Medicines and Cosmetics—"They've Got to Be Good!" is mere wishful thinking; such chapter headings as "Read Schlink and Be Leery" are funny but far less amusing than some of the text of the book. The author discusses the American Medical Association in part as follows: "Some proprietary medicines which have long had a large sale, have been accepted by the consumer, and found to be efficacious in relieving minor afflictions, are, and have always been classed as nostrums by the Association. The reason is not far to seek. Self-medication, or any product that makes self-medication possible . . . deprives the doctor of some revenue, so from that angle there is naturally some objection to it regardless of whether the particular medicine is more profitable or satisfactory to the consumer than the service of a doctor." These statements display such ignorance that they do not deserve consideration. Is it possible that the author knows nothing about the medical profession's active part in disease prevention and public health? The dangers of self-medication are not detrimental to the doctor's income but rather to the health and welfare of the patient. The American Medical Association has led the way in the fight against dangerous "patent medicines" so that actually self-medication may be somewhat less hazardous than at one time, but it is still frequently disastrous. The author is apparently unaware of the fact that the Council on Pharmacy and Chemistry of the American Medical Association permits advertising directly to the public of certain types of its accepted products when it is in the interest of the public to do so, as for example antiseptics. There is a chapter on "How the Government Protects Us" which cites seizures under the violations of the Food and Drug Act. The book concludes with two chapters, one on "Big Business" which ends with a section on "How Much We Owe to 'Big Business,'" and a final chapter which is a boost for "The Druggist—Your Good Friend." Errors in this volume do not inspire confidence, and misrepresentation of fact indicates unfamiliarity with the subjects. Some of the statements are as far from reality as the author's "bugbear" which looks like a cross between a bear and a grasshopper. It may be granted that consumers' protective organizations have certain faults, but there is no excuse for the promotion of the utopian opinion of commercial altruism which this author seems to hold. It is interesting to note the comment of some of the "Big Business" which he glorifies. *Drug and Cosmetic Industry* concludes its review of this book as follows: "As is often the case, cosmetics, drugs and foods may suffer more from the intemperate defenses of friends than from attacks of their avowed enemies."

Les acquisitions nouvelles de l'endocrinologie. Par B. Rivoltre. Third edition. Paper. Price, 45 francs. Pp. 264, with illustrations. Paris: Masson & Cie, 1937.

The first edition of this interesting work appeared in 1931. In opening the present edition the author remarks on the immense progress achieved in endocrinology during the decade since his first publications in the field. With characteristic French pride he refers to the satisfaction from the proportionately large contributions, physiologic, biochemical and clinical, made by French physiologists, physicians and surgeons. Ten years ago theories were prominent, their bulk now gratifyingly reduced or replaced by ascertained relevant facts. The first fifty-seven pages expound developments in parathyroid endocrinology. From the fatal tetany formerly inevitable in laboratory dogs after parathyroid removal, valuable and gratifying control of experimental results have been secured by ascertaining the mutual relations and interchanges of the calcium and

the phosphorus content in the blood. American physiologists are credited with "profound analyses of the mineral interchanges involved in studying minutely the influence of food regimens upon the phospho-calcic exchanges in tetanous animals." The eighth and final chapter, of 59 pages, points out the momentous developments in endocrinology of the hypophysis, with their significant influence on the thyroid. Intervening chapters set forth adrenal, pancreatic, thymic endocrine problems and experiments, together with those of the sex glands, male and female. Much discussion of Addison's disease occurs in connection with cortico-adrenal discoveries. The efficient salt solution therapy evolved was first published by Professor Acland and Rivoire in the author's first edition, 1931. Space is also given (p. 98) to "a recent discussion in Chicago in the Central Society of Clinical Research, where Snell and Kepler on the one side and Hoffmann and his pupils on the other reported uniformly favorable results obtained with the cortical extract of Kendall, and that of the Wilson Laboratory. Kendall, however, had never observed cortical resistance to his extract in Addison's disease." Rivoire declares impartially for the two extracts, adding a third from Amsterdam and regretting the absence of an "active" French preparation. No bibliography appears in this work; authors are referred to merely by name, though some are dated, as "Zondek, 1931," "Iscovesco, 1912," "Smith, 1921."

Surface and Radiological Anatomy for Students and General Practitioners. By Arthur B. Appleton, M.A., M.D., Professor of Anatomy in the University of London, William J. Hamilton, M.D., B.Ch., D.Sc., Professor of Anatomy in the University of London at the Medical College of St. Bartholomew's Hospital, London, and Ivan C. C. Tehaperoff, M.A., M.D., B.Ch., Assistant Radiologist at St. Thomas's Hospital, London. Cloth. Price, \$5.50. Pp. 311, with 338 illustrations. Baltimore: William Wood & Company, 1938.

The authors endeavor to provide an introduction to the study of anatomic features which are accessible to examination in the living subject, and to the usual methods of physical examination they have added radiology. By the extensive use of illustrations in this book they were able to coordinate radiologic anatomy with those features which can be determined by external examination and with those other details which can be determined only by dissection. The book is arranged in sections corresponding with the parts in which the body is usually dissected, and some blank pages for notes have been included. Some general consideration is also given to radiologic technic, which they believe necessary for the interpretation of the roentgenograms. They omit detailed descriptions of the attachments of individual muscles but emphasize the coordinated production of movement and maintenance of posture. The book shows the surface contours in relation to the underlying structures to elucidate especially the more difficult radiologic appearances. The roentgenograms have been reproduced as negatives in view of the general practice of examining original roentgenograms in this form.

Workbook in Elementary Diagnosis for Teaching Clinical History Recording and Physical Diagnosis. By Logan Clendening, Professor of Clinical Medicine, University of Kansas. Cloth. Price, \$1.50. Pp. 167, with illustrations. St. Louis: C. V. Mosby Company, 1938.

According to the author, this book is intended as a workbook in elementary diagnosis covering a course for sophomore medical students. The student should readily acquire the routine of history recording and learn the methods of physical examination on reading this textbook because the subject is presented simply. There are a few errors which might be corrected; for example, it is definitely an error to define a thrill as just what the name implies—it is a grating feeling and a crepitation and at the same time to describe "a thrill as similar to a feeling as when your hand is on the neck of a purring cat." "Point of Maximum Impulse (PMI) is not the apex but is caused by the impact of the flat of the ventricle" should be more definitely referred to the left ventricle and the "flat" omitted. In the description of palpation of the abdomen it is regrettable to note a failure of the author to begin with the palpation of the normal abdomen and the failure to mention the necessity for gentleness during examination in the normal and abnormal condition of the abdomen. The chapter devoted to examination of children and infants is commendable. The author has unquestionably succeeded in making the entire text elementary. It is questionable whether so ele-

mentary a presentation for sophomore medical students is necessary. The pen and ink drawings, while beautifully executed and in keeping with the idea of a primer, do not convey as much as photographs. The exercises at the end of the book complete the idea of an elementary textbook but it is questionable whether a sophomore student will profit by an exercise such as naming twenty diseases in which there are enlargements or masses in the neck. This book is distinctly pedantic in type and therefore is not in keeping with the more liberal trend in medical teaching.

How to Live: Rules for Healthful Living Based on Modern Science. By Irving Fisher, LL.D., and Haven Emerson, M.D., Professor of Public Health Practice, Columbia University. Prepared in collaboration with the Hygiene Reference Board of the Life Extension Institute and the Advisory Board of the Vitality Records Office. Twentieth edition. Cloth. Price, \$2.50. Pp. 422, with illustrations. New York & London: Funk & Wagnalls Company, 1938.

This volume is now in its twentieth edition. This edition is dedicated to Dr. Eugenc Lyman Fisk, who was co-author in all earlier editions. In the preparation of the new edition members of the reference board collaborated, so that it may be presumed that all of them take some of the responsibility for what is contained in this volume. There are also a considerable number of appendixes devoted to specific subjects in which individual authors take the responsibility. Unfortunately, the work has not been sufficiently revised to eliminate several ridiculous statements which appear in the text. For example; In the illustration between pages 8 and 9 it is said that the wearing of shoes with pointed toes leads to anemia, indigestion and poor circulation. On page 38 it is said that an ample diet includes raw fruits, raw nuts, raw greens and dairy products, and that such a diet provides every essential of complete nutrition for the average person. On page 42 it is said that the proteins of meat are less perfect than the proteins of nuts and greens. On page 56 the suggestion is made that the average person obtain litmus paper from a drug store and test his urine to see if it is acid or alkaline; and, indeed, it is urged that he do so to keep his urine neutral—a suggestion which is certain to create a good many urinary hypochondriacs. On page 58 appears the strange notion that canned foods are practically devoid of vitamins and that when people camp out and live on canned foods they become vitamin hungry so that they develop a special craving for vitamins. Where is the scientific evidence to support this notion? Also a holdover from a period of superstition in diet are those sections of the book concerning the eating of meat and the hygiene of the colon. These special views are not held by the majority of scientific physicians. Pages 396-402 are occupied by testimonials in favor of some of the peculiar notions expressed in the pages that have been especially mentioned. The chapter dealing with alcohol and tobacco is full of nonsense. Fortunately the articles which appear in the appendixes and which constitute about half the book may be considered as individual contributions for which only their authors are responsible. There it becomes clear what part has been played in the adoption of some of these views by the proponents of certain special concepts in the field of health.

Previous editions of this book have sold almost 450,000 copies. Perhaps by the time the twenty-first edition is reached a real revision and modernization may be provided.

Chemistry of the Brain. By Irvine H. Page, A.B., M.D., Hospital of the Rockefeller Institute for Medical Research, New York. Cloth. Price, \$7.50. Pp. 444. Springfield, Illinois, & Baltimore: Charles C. Thomas, 1937.

This volume represents a summary of the present state of our knowledge concerning brain constituents and their metabolism. There are extended and valuable references, particularly to the more recent investigations in the general field of intermediary metabolism, so that the scope of the work is considerably greater than its title would indicate. There is an excellent historical introductory chapter, followed by a more extensive survey of the chemistry and metabolism of various brain constituents. A comprehensive chapter on brain oxidations has been contributed by Dr. J. H. Quastel of the Cardiff Mental Hospital. The purely chemical aspects of brain constituents are treated briefly, the emphasis being on their correlation as far as possible with metabolic function. The clinical aspects of the problem are not neglected and the book

should prove of interest not only to the laboratory investigator but to the clinician as well. The organization and critical interpretation of the large amount of data included in the book is a task of considerable difficulty, and it is doubtful whether the present status of our knowledge of many of the topics treated is sufficient to permit a treatment of the data that would be universally acceptable. On the whole, however, the treatise represents a valuable contribution to biochemical and biologic literature.

Medical State Board Questions and Answers. By R. Max Goepff, M.D. Seventh edition. Cloth. Price, \$5.50. Pp. 644. Philadelphia & London: W. B. Saunders Company, 1938.

This book offers concise answers to the actual questions asked at state board examinations in all the forty-eight states and by the National Board of Medical Examiners. Since 1929, when the previous edition was published, there have been so many advances in medicine that a new edition was considered advisable. The changes were so numerous that the type was entirely reset. The author was assisted in this work by Dr. Frederick S. Baldi in medical jurisprudence, Dr. Abraham Cantarow in bacteriology, Dr. Calvin M. Smyth Jr. in surgery and gynecology, and Dr. Robert P. McCombs for the selection of material. The questions and answers are arranged under the general headings of anatomy, physiology, physiologic chemistry, pathology, bacteriology, materia medica and therapeutics, practice of medicine, surgery, obstetrics and gynecology, hygiene and medical jurisprudence. There is an extensive index, which is an indispensable feature of the book if it is to be used as a reference volume. In their effort to be concise, perhaps the authors occasionally trimmed some of the answers too closely. On page 24 is the question Name the endocrine glands. The answer given is "spleen, suprarenal bodies, glandulae caroticae (O. T. intercarotid bodies), thyroid and parathyroid, thymus, glomus coccygeum."

Practical Clinical Gynecology. By Henry C. Falk, M.D., F.A.C.S., Clinical Professor of Gynecology, New York University College of Medicine. Cloth. Price, \$5. Pp. 393, with 190 illustrations. New York: American Journal of Surgery, Inc., 1938.

This volume is apparently intended to convey a smattering of gynecology to practitioners who have forgotten what they were taught in medical school. The book is written informally, with frequent use of questions and answers. Much of the writing is loose. Many of the principles enunciated are entirely contrary to the best gynecologic practice of today. There is no evidence of the author's familiarity with many important gynecologic studies published in the last ten years. The illustrations are in no way impressive. The scope of the work is exemplified by the chapter on carcinoma, which in a scant fourteen pages covers (after a fashion) the cause, course, signs, symptoms, histologic diagnosis, clinical diagnosis and treatment of carcinoma of the uterus (cervix and fundus). The treatment of carcinoma is described in two sentences. Retroperitoneal erysipelas is mentioned, but there is no discussion of dropsy of the ovary. The volume is not recommended for nurses, undergraduate students, postgraduate students or gynecologists. It is poorly organized, incomplete and in many places unsound.

Thirty Years After: The Story of the Class of 1908, Medicine, of the University of Pennsylvania in the Thirty Years That Have Elapsed Since Leaving the Medical School [Including Portraits]. Data compiled by J. H. Musser, M.D. Cloth. Pp. 114, with illustrations. New Orleans: Wetzel Printing, Inc., 1938.

This is the story of a class which graduated thirty years ago from the University of Pennsylvania School of Medicine. There is a brief biography accompanied by a picture of each living member of the class of 1908, of which there are 111, thirty-three of the members having died since graduation. There is also a statistical analysis which brings out some interesting facts. Four of the members of the class of 1908 have not married; ninety-two married men of the class have a total of 181 children, or a little less than two children per marriage. Of these 181 children, forty-two, or 25 per cent, are either already doctors or are going into medicine. At the end of ten years the average income of sixty-four men in the class was \$6,787. At the end of twenty years the average income of sixty-one men of this class was \$15,803. At the end of thirty

years after graduation the average income of sixty-six men was \$13,157. Nearly all the members reported a decrease in their financial returns from practice at the end of thirty years as compared with the end of twenty years. The author further analyzes the financial returns of the class with regard to whether they were general practitioners or specialists. The class has quite a remarkable teaching record, twenty-four of the 101 who answered this part of the questionnaire having obtained the rank in medical schools of either associate, assistant or full professor. Only nine of the living members of the class, however, are listed in "Who's Who." Among the hobbies and recreations, golf heads the list with thirty-six, tennis claims eight, baseball one, polo four, stamp collecting six, photography four, bridge four and poker one. There is a list of the deceased members of the class with brief data obtained chiefly from the obituary columns of THE JOURNAL.

A Text-Book of Bacteriology for Dental Students. By Arthur Bulleid, L.R.C.P., M.R.C.S., L.D.S., Dental Surgeon and Lecturer in Special Bacteriology to the Dental School, Guy's Hospital. Second edition. Cloth. Price, 15s. Pp. 207, with 77 illustrations. London: William Heinemann, Ltd., 1938.

The scope of this book is limited, although the author hopes "that it is comprehensive enough to give the student an insight into general bacteriology, with special application in his own sphere, viz.: the mouth." The size and content hardly warrant this claim and it is recommended rather as a supplement to the more comprehensive textbooks of bacteriology in rather general use. Technical methods and culture mediums are adequately covered; the portion concerning those specially adapted for use in studying the oral flora is highly commended. Pathogenic bacteria are disposed of in two chapters and the same amount of space is given to the subjects of immunity, vaccines and antisera. The section on the original bacteriology of caries has a number of faults. In it the author has failed to draw a sharp line between the past and the present. The inclusion of lengthy descriptions of organisms such as *B. gingivae pyogenes* and *B. plexiformis* taken from the works of Miller and Goadby is hardly warranted, since it is not possible to reconcile these names and descriptions with those used in modern textbooks on determinative bacteriology. The chapter on blood examinations and cell counts is probably out of place in a textbook on bacteriology.

Psychiatric Nursing. By William S. Sadler, M.D., Chief Psychiatrist and Director, The Chicago Institute of Research and Diagnosis, Chicago. In collaboration with Lenn K. Sadler, M.D., Associate Director, The Chicago Institute of Research and Diagnosis, and Anna B. Kellogg, R.N., Chief of Nurses, The Psychiatric Clinic of the Chicago Institute of Research and Diagnosis. Cloth. Price, \$2.75. Pp. 433, with 19 illustrations. St. Louis: C. V. Mosby Company, 1937.

The book is divided into major chapters concerned with the history of psychiatry, the anatomy of the nervous system, an extensive chapter on considerations of neuroses and psychoses, the chapters dealing more specifically with nursing of various cases. Although the chapters on the neuroses are extensive, the classification of them is quite confusing and the various types overlap one another a great deal. The mechanisms are discussed from a rather simple psychobiologic point of view with a good deal of common sense. The psychoses are discussed along the orthodox lines. The presentation of the material is quite simple and undoubtedly can be easily absorbed by the average nurse. The last chapters of the monograph are very satisfactory. In the special problems of psychiatric nursing the author covers extensively the various emergencies and problems which come to the attention in treatment of psychiatric cases. There is a valuable chapter on therapy as used by a nurse and there is an excellent chapter on the personality of a nurse in the relation to the patient. On the whole this is a satisfactory manual for young women interested in psychiatric nursing.

Illustrations of Anatomy for Nurses. By E. B. Jamieson, M.D., Senior Demonstrator and Lecturer, Anatomy Department, University of Edinburgh. Paper. Price, \$3. Loose-leaf. 62 plates. Baltimore: William Wood & Company, 1938.

This volume is a condensation of the book called "Illustrations of Regional Anatomy" which has been prepared for doctors and medical students. Sixty-two of the plates from the larger book are included in the special volume for nurses.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Medical Practice Acts: Administration of Anesthetics by Nurse Under Direction of Dentist.—The appellee, a dentist, brought this suit in the superior court of Maricopa County, Ariz., against the state of Arizona and its attorney general, and the county attorney of Maricopa County, in their official capacities, for a declaratory judgment to determine his right to employ a nurse anesthetist. He alleged that in his practice it was frequently necessary to give a patient a general anesthetic and that he desired to employ a registered nurse, who had taken a prescribed course of anesthesia at a hospital in good standing, to administer the anesthetic under his direction and in his immediate presence. A question had arisen, however, as to whether such administration by a registered nurse was lawful and he desired an opinion from the court with respect to the matter. The superior court gave judgment to the effect that the course of conduct which he intended to follow was lawful, and the state appealed to the Supreme Court of Arizona.

The Arizona law regulating the practice of registered nurses contains the following provision:

A registered nurse may administer anesthetics under the direction of and in the immediate presence of a licensed physician or surgeon, provided such nurse has taken a prescribed course of anesthesia at a hospital in good standing, or is a graduate in the science of anesthesia from some recognized school or college.

The specific question considered by the court was whether a dentist, duly licensed to practice dentistry, was a "licensed physician or surgeon" within the meaning of the section just quoted, or whether for the purpose of that section these words mean a person who is licensed to practice medicine generally. The dental practice act, enacted in 1935, the court pointed out, for the first time expressly authorized dentists, in the practice of dentistry, to administer anesthetics. Before that time there was grave doubt whether under the law a licensed dentist could legally do so and it was the general practice, when such an administration was necessary, to call in a regular physician. It was clear to the court that the reason for the express inclusion in the 1935 dental act of the administration of anesthetics in the course of dental surgery as one of the things which a dentist was expected and permitted to do as a part of the regular practice of his profession was to remove any possible question as to his right to do so. There could be no question, therefore, that if the dentist in the present case himself, or any other licensed dentist, desired to administer an anesthetic to a patient, as a part of dental practice, they would be fully within their right under the law. It was contended however that while a dentist may administer the anesthetic himself, he may not permit a registered nurse to do it under his direction and in his immediate presence.

If, continued the court, a limited meaning is given to the words "physician or surgeon" as used in the law regulating the practice of nursing, the dentist in the present case was not a physician or surgeon within such meaning and therefore could not use a registered nurse to administer an anesthetic. But the legislature by the dental practice act of 1935 expressly gave to dentists the right personally to administer such treatment. Necessarily, by so doing, the legislature determined that a licensed dentist is fully qualified to administer an anesthetic in dental operations, which means that he knows not only how but when to give it. A licensed physician and surgeon can know no more, in the opinion of the court. To hold then that a qualified nurse may administer anesthetics in a dental operation under the direction of one man, when she may not under that of another who is equally qualified to direct her, would be to assume that the legislature had meant to permit one class of practitioners to do a certain thing, while prohibiting another class, equally qualified so far as the protection of the public health is concerned, from doing that

same thing. To give the section in the nursing practice act that meaning would be to give a practical monopoly, the court thought, of the administration of anesthetics in dentistry to licensed physicians and surgeons and thus render the act invalid as an exercise of the police power. To hold, on the other hand, that the word "surgeon" as used in the nursing act includes a "dental surgeon" would make it a proper and legitimate exercise of that power. Under such circumstances, the court pointed out, every rule of statutory construction required that it be given the constitutional, rather than the unconstitutional, meaning. It was the opinion of the court, therefore, that registered nurses in Arizona may administer anesthetics under the direction and in the immediate presence of a licensed dental surgeon for the purpose of assisting in any of the operations which such surgeon is authorized to perform. The judgment of the superior court was affirmed.—*State v. Borah (Ariz.)*, 76 P. (2d) 757.

Attorneys: Disbarment for Soliciting Personal Injury Cases Through Physicians.—On the petition of the Queens County Bar Association, disciplinary proceeding was brought in the supreme court of New York, appellate division, second department, against the defendant attorney, charging him with soliciting negligence cases or personal injury cases through physicians, policemen and others and paying such persons for procuring retainers for him. The court held that the records showed that the defendant had not only engaged in the activities charged but had resisted the charges and testified falsely. The defendant, said the court, was guilty of flagrant violations of duty as an attorney and was no longer entitled to engage in the practice of law. Accordingly, the court disbarred the defendant and ordered his name struck from the roll of attorneys.—*In re Glickman (N. Y.)*, 1 N. Y. S. (2d) 885.

Malpractice: Liability of Naturopath and Nurse for Burns Due to Diathermy Treatment.—The plaintiff was suffering from a painful swelling in the muscles of the right side of her neck and consulted the defendant naturopath. After examining the plaintiff, the naturopath prescribed a diathermy treatment, which was administered by the defendant nurse, an office assistant of the naturopath. As a result of the treatment, the plaintiff sustained a superficial burning and blistering of the skin over a considerable portion of her abdomen and a deep third degree burn about 3 inches in diameter in and around her umbilicus. She sued the naturopath and his nurse for damages. The trial court gave judgment against the naturopath but directed a verdict for the nurse, on the ground that she was not personally liable for the results of her negligence, if any, in the operation of the diathermy machine. The plaintiff excepted to the action of the trial court in thus instructing the jury to return a verdict for the nurse and appealed to the Supreme Court of Oregon.

On appeal, the nurse contended that the complaint did not state facts sufficient to constitute a cause of action against her. The complaint, observed the court, charged that the defendants administered the treatment in a careless and negligent manner, and as a direct result of this carelessness and negligence the plaintiff sustained the injuries of which she complained. If a complaint contains general allegations of negligence and carelessness, the court said, it is not essential that the details be set forth in it. This was an action for malpractice and the cause of action alleged in the complaint was a tort. In *Wemelt v. Mount*, 134 Ore. 305, 292 P. 93, the plaintiff had been burned during the course of diathermy treatments administered by a lay employee of the defendant physicians. The court in that case said:

This act is one of tort and all the defendants who participated or are responsible for the act are liable severally.

The complaint in the present case was, in the opinion of the court, sufficient. The lower court practically found that the defendant nurse was negligent and that she was not liable for her negligence but that the naturopath was. But, said the court, the nurse was not relieved from liability for her negligence because she was acting under the direction of her superior, the naturopath. In certain instances a nurse or office assistant of a physician might innocently injure a patient

without knowledge that her conduct would result in such injury. In the present case, however, the testimony tended to show that the nurse was fully aware of the results that follow the application of excessive current. A person who operates an x-ray or similar electrical appliances used in healing is required to use that degree of care, diligence and skill ordinarily possessed by similar operators in similar communities. The rules governing the duty and liability of physicians and surgeons in the performance of professional services are applicable to practitioners of the kindred branches of the healing art, such as dentists, oculists and manipulators of x-ray machines and like apparatus.

In the opinion of the Supreme Court, therefore, the trial court erred in not submitting the case as to the nurse to the jury. The judgment of the trial court in this respect was reversed and the cause remanded for further proceedings.—*Wood v. Miller et al. (Or.)*, 76 P. (2d) 963.

Drugs: Gauze Bandage a Drug Under the Federal Food and Drugs Act of 1906.—The claimant shipped packages of gauze bandages from Connecticut to a consignee in New York City. The bandages were in small packages contained in larger cartons, which were labeled, as were the small packages, to the effect that the gauze was sterilized. Each small package bore also a guaranty stating that the product had been "scientifically prepared for surgical use under the most sanitary manufacturing conditions." The gauze was not, however, sterilized or fit for surgical use but contained "living bacteria consisting of gram-positive sporeforming bacilli and nonspore-forming bacilli, gram-positive and gram-negative bacilli, capable of growing aerobic conditions and anaerobic bacteria." The shipment was seized under the federal food and drugs act and a libel proceeding filed in the district court for the southern district of New York to have condemned and declared forfeited the forty-eight packages comprising the shipment. The district court entered a decree of condemnation and forfeiture and the claimant appealed to the United States circuit court of appeals, second circuit.

The question on appeal was whether such a substance as a gauze bandage was within the scope of the federal Food and Drugs Act and so subject to seizure and forfeiture. That act, in section 6, defines the term drug as follows:

The term "drug," as used in sections 1 to 15, inclusive, of this title, shall include all medicines and preparations recognized in the United States Pharmacopeia or National Formulary for internal or external use, and any substance or mixture of substances intended to be used for the cure, mitigation, or prevention of disease of either man or other animals.

If a gauze bandage is within the act at all, the court said, it must fall within its purview as a "substance . . . intended to be used for the cure, mitigation, or prevention of disease of either man or other animals." In the opinion of the court, a gauze bandage was such a substance. The claimant argued, however, that the meaning of the word "substance" must be held to be somewhat narrowed, under the principle of ejusdem generis, by words used in the statute in connection with it. But the application of that principle, the court said, did not help the claimant's cause in this particular case. Among those things recognized in the United States Pharmacopeia as "preparations" are absorbent cotton and adhesive plaster made by spreading the adhesive on cotton cloth. This recognition of absorbent cotton, a substance generally similar in composition and use to gauze bandage, sufficiently indicated to the court that the latter, while not itself recognized, was of a kind not dissimilar from a substance that was recognized. That made it, the court thought, exactly the sort of thing Congress must have intended to include in the general language which was put there for the very purpose of making the statute cover more substances of the kind mentioned than were actually recognized in the Pharmacopeia or National Formulary.

The act, continued the court, was passed to prevent injury to the public health. It should be given a fair and reasonable construction to attain its aim. Gauze bandages, clearly intended for surgical use, are a menace to the public health when misbranded to show that they are sterilized. In the present case the gauze bandages were not fit for the use for which their labels

falsely represented them to have been prepared and so were subject to condemnation and forfeiture.

The judgment of the district court against the claimant was affirmed.—*United States v. 48 Dozen Packages, More or Less, of Gauze Bandage Labeled in Part Sterilized*, 94 F. (2d) 611.

Malpractice: Burns from Hot Pack-Off Placed on Patient's Abdomen.—The defendant, a physician, performed an abdominal operation on the plaintiff during the course of which a hot pack-off was placed on the patient's abdomen and a burn resulted. She thereafter sued the defendant in the superior court, Androscoggin County, Maine, but subsequently the case was withdrawn from the jury and, with the consent of the parties, presented to the Supreme Judicial Court of Maine for determination.

From the evidence, the court said, a jury could properly infer that while the patient was under the influence of ether and still on the operating table, the pack-off was laid on her abdomen and a burn resulted. There was nothing, however, warranting a finding that the defendant placed the pack-off on his patient's abdomen. Nor was there any showing that in the exercise of that degree of care and skill required of him, with constant guard against possible complexities, he could have discovered the pack-off. Its application did not appear to have been known to him until his patient was back in her own hospital room, when the fact that she had been burned was called to his attention. The presence of the pack-off was quite as likely to have been due to the fault of others, the court said, as to any act, either of commission or of omission, of the defendant. Strikingly similar to the present case in essential principles, the court pointed out, was *Guell v. Tenney*, 262 Mass. 54, 159 N. E. 451. In that case, one of tort against a surgeon who, at a private hospital, performed an appendectomy and allegedly did not remove a sponge before closing the incision, the court said:

The nurses who were present at the operation were employed by the hospital. There was no evidence to show that any of the persons present at the operation were servants or agents of the defendant. . . . It may fairly be inferred that, in the performance of an operation of this character in a hospital, nurses are commonly present to assist the operating surgeon. . . .

As there was no evidence that the nurses or other persons present and assisting were servants or employees of the defendant, he cannot be held responsible for [any negligence on their part].

So in the present case the court thought that the doctrine of respondent superior did not apply and that the judgment should be for the defendant.—*Watson v. Fahey (Maine)*, 197 A. 402.

Society Proceedings

COMING MEETINGS

- Academy of Physical Medicine, Washington, D. C., Oct. 24-26. Dr. Herman A. Osgood, 144 Commonwealth Ave., Boston, Secretary.
- American College of Surgeons, New York, Oct. 17-21. Dr. George W. Crile, 40 East Erie Street, Chicago, Chairman, Board of Regents.
- American Public Health Association, Kansas City, Mo., Oct. 25-28. Dr. Reginald M. Atwater, 50 West 50th St., New York, Executive Secretary.
- American Society of Tropical Medicine, Oklahoma City, Nov. 15-18. Dr. E. Harold Hinman, Wilson Dam, Ala., Secretary.
- Associated Anesthetists of the United States and Canada, New York, Oct. 17-21. Dr. F. H. McMechan, 318 Hotel Westlake, Rocky River, Ohio, Secretary General.
- Association of American Medical Colleges, Syracuse, N. Y., Oct. 24-26. Dr. Fred C. Zapffe, 5 South Wabash Ave., Chicago, Secretary.
- Central Society for Clinical Research, Chicago, Nov. 4-5. Dr. Lawrence D. Thompson, 4932 Maryland Ave., St. Louis, Secretary.
- Inter-State Postgraduate Medical Association of North America, Philadelphia, Oct. 31-Nov. 4. Dr. W. B. Peck, 27 East Stephenson St., Freeport, Ill., Managing Director.
- Omaha Mid-West Clinical Society, Omaha, Oct. 24-28. Dr. J. D. McCarthy, 107 South 17th St., Omaha, Secretary.
- Pacific Coast Society of Obstetrics and Gynecology, Los Angeles, Nov. 30-Dec. 3. Dr. T. Floyd Bell, 400 29th St., Oakland, Calif., Secretary.
- Radiological Society of North America, Pittsburgh, Nov. 28-Dec. 2. Dr. Donald S. Childs, 607 Medical Arts Bldg., Syracuse, N. Y., Secretary.
- Southern Medical Association, Oklahoma City, Nov. 15-18. Mr. C. P. Loranz, Empire Bldg., Birmingham, Ala., Secretary.
- Southern Surgical Association, White Sulphur Springs, W. Va., Dec. 6-8. Dr. Alton Ochsner, 1430 Tulane Ave., New Orleans, Secretary.
- Southwestern Medical Association, El Paso, Texas, Oct. 27-29. Dr. Orville E. Eghert, First National Bank Bldg., El Paso, Texas, Secretary.
- Western Surgical Association, Omaha, Dec. 2-3. Dr. Albert H. Montgomery, 122 South Michigan Blvd., Chicago, Secretary.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1928 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but may be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

Alabama State Medical Assn. Journal, Montgomery

8: 61-96 (Aug.) 1938

Insurance Triangle: Applicant, Examiner, Company. B. F. Byrd, Nashville, Tenn.—p. 61.

Chlorionepithelioma. H. B. Dowling, Mobile.—p. 64.*

*Atabrine as Malarial Prophylactic Agent: Experiment with Drug in a Region in Central Alabama. D. G. Gill, Montgomery, and M. Smith, Tuskegee.—p. 66.

Asthma: Treatment with Iodized Oil: Report of 103 Cases. J. F. Alison, Selma.—p. 68.

Atabrine as Malarial Prophylactic.—The efficacy of atabrine in preventing clinical attacks of malaria was studied in an area located in Macon County, Ala. The area was divided into two approximately equal and similar parts. To the inhabitants of one part Gill and Smith gave doses of 0.025 Gm. of atabrine to children and 0.15 Gm. to adults twice a week, while those of the other part received no prophylactic medication, thereby serving as controls. The atabrine given on two non-consecutive days of each week was instrumental in reducing the blood parasite index from 22.9 to 3.4 per cent over a period of five months—from June to November. During the same time the index of the control group decreased from 13 to 4.6 per cent. Atabrine was administered a maximum of forty-three times to the 726 persons in the prophylactic group, the average number of administrations per person being 36.6. The number of clinical attacks of malaria in the prophylactic group was twelve during the entire season, as compared with ninety-six clinical attacks in the control group not receiving atabrine. Of the twelve cases of malaria occurring in the prophylactic group, more than one half occurred in July. After July the incidence in the prophylactic group fell rapidly, reaching nil in October, while during this month eleven cases appeared in the control group.

American Journal of Hygiene, Baltimore

28: 149-320 (Sept.) 1938

Study of Larval Chetotaxy of Anopheles Walkeri Theobald. H. S. Hurlbut, Ithaca, N. Y.—p. 149.

Malaria in the Panama Canal Department, United States Army: II.

Results of Treatment with Quinine, Atabrine and Plasmodochin. C. J. Gentzkow and G. R. Callender, Ancon, Canal Zone.—p. 174.

Description of Shock Disease in the Snowshoe Hare. R. G. Green, Minneapolis, and C. L. Larson, Washington, D. C.—p. 190.

Method for Measuring the Rate of Elimination of Bacteria from the Human Mouth. J. L. T. Appleton, Philadelphia; H. Klein, and C. E. Palmer, Washington, D. C.—p. 213.

Epidemiology of Malaria in Eastern Redwings (Agelaius P. Phoeniceus). C. M. Herman, Baltimore.—p. 232.

*Neonatal Mortality by Order of Birth and Age of Parents. J. Yerushalmy, Albany, N. Y.—p. 244.

Ingestion of Red Blood Cells by Endamoeba Coli and Its Significance in Diagnosis. E. E. Tyzzer and Q. M. Geiman, Boston.—p. 271.

Effect of Trichomonas Fetus on Tissue Culture Cells. Mary Jane Hogue, Philadelphia.—p. 288.

Mortality of Merozoites in Infections with Plasmodium Cathemerium in Canaries. R. Hegner and Lydia Eskridge, Baltimore.—p. 299.

Common Duck as Convenient Experimental Host for Avian Plasmodium Fruma Wolfson, Baltimore.—p. 317.

than 3 per cent of the infants surviving the first month of life were premature. The frequency of prematurity was 42.9 per thousand live births. The mortality of premature births was extremely high (389.2), and it rose with the order of birth. The neonatal mortality of infants carried to full term was only 15.2 per thousand live births. The neonatal mortality for male infants was considerably higher than for female infants for every order of birth. Premature births were more frequent in urban communities than in the rural part of the state. However, the mortality among the premature was higher in the rural areas than in the cities. The neonatal mortality of infants born to young mothers and to older mothers is considerably higher than that of infants born to mothers aged from 20 to 30. The lowest rate was recorded for mothers aged from 27 to 28. The same trend of mortality by the age of the mother was observed in practically every order of birth. It started high for young mothers of every birth order, dropped gradually to a minimum and then rose to high rates for old mothers. Neonatal mortality seems to be independently correlated with the order of birth and the age of the mother. Neonatal mortality was found to be closely associated with the age of the father. This association was not due only to the high correlation that exists between the age of the father and age of the mother for, when the age of the mother was held constant, the variation of neonatal mortality with the age of the father was definite. It started high for young fathers, dropped to a minimum, and rose thereafter with the age of the father. The optimal age group of fathers was from 25 to 29.

American J. Obstetrics and Gynecology, St. Louis

36: 183-362 (Aug.) 1938

*Experimental Production of Ovulation in the Human Subject. M. E. Davis and A. K. Koff, Chicago.—p. 183.

Study of Water, Sodium and Energy Exchange During the Latter Part of Pregnancy. R. H. Freyberg, R. D. Reekie and C. Folsome, Ann Arbor, Mich.—p. 200.

One Stage Operation for Resection of Rectosigmoid and Rectum for Carcinoma (With or Without Hysterectomy): I. Combined Anterior and Posterior Resection; II. Combined Abdominoperineal Resection. J. P. Pratt, Detroit.—p. 209.

*Further Observations on Role of Streptococcus in So-Called Trichomonas Vaginalis Vaginitis. G. F. Hibbert and F. H. Falls, Chicago.—p. 219.

Consideration of Artificial Fever Therapy and Sulfanilamide Therapy in Treatment of Gonorrheal Infections of Women. L. M. Randall, F. H. Krusen and E. G. Bannick, Rochester, Minn.—p. 230.

Artificial Fever Therapy in Pelvic Inflammatory Disease. M. A. Darling, J. M. Berris and M. Newman, Detroit.—p. 238.

Effect of Quinine on Auditory Nerve. R. A. West, Wichita, Kan.—p. 241.

Sterilization of Obstetric Patients in Vanderbilt University Hospital 1925-1937. G. S. McClellan and L. E. Burch, Nashville, Tenn.—p. 249.

*Study of 288 Primiparas Over the Age of 35 Compared with 300 Primiparas Under the Age of 25. C. E. Galloway and T. D. Paul, Evanston, Ill.—p. 255.

Pelvic Measurements of 4,144 Iowa Women. W. F. Mengert, Iowa City.—p. 260.

Management of Placenta Praevia: Analysis of 47,828 Cases. D. Findley, Omaha.—p. 267.

Analysis of Human Ovotestis: Associated with Congenitally Bisected Uterus Herniated into Inguinal Canals. J. R. Reinberger and C. S. Simkins, Memphis, Tenn.—p. 275.

Intraligamentary Pregnancy: Survey of All Published Cases of Over Seven Calendar Months, with Discussion of Additional Case. P. K. Champion, Dayton, Ohio, and Nicola J. Tessitore, New Orleans.—p. 281.

Observations on Intra-Uterine Pressure During First Stage of Labor. J. P. Salerno, Houston, Texas.—p. 294.

Cystic Endometrial Changes in Ovulatory Cycles: Mixed Endometrium. L. Wilson and R. Kurzrok, New York.—p. 302.

Full Term Abdominal Pregnancy with Recovery of Both Mother and Baby. W. D. Crecca and R. A. Cacciarelli, Newark, N. J.—p. 312.

Production of Ovulation.—In order to determine whether ovulation in the human being could be produced, Davis and Koff administered the gonadotropic fraction obtained from the urine of pregnant mares to thirty-six women who were to be subjected to laparotomy for a variety of pathologic conditions. Many of the subjects were at the period in life in which there is a rapid decrease of ovarian activity. Others had pathologic conditions which would mask any results which might be obtained. The lapse of time between the administration of the substance and the inspection and removal of the ovaries varied. The duration of time that elapsed from the administration of the substance until ovulation was produced was unusually short. It is probable that in many of the experiments maturing follicles

were already present, so that completion of the process resulting in ovulation was rapid. On the other hand, in the women who were in the latter half of the cycle, maturing follicles ordinarily should not have been present and yet rapid ovulations took place. The authors are of the opinion that this substance is capable of causing rapid growth of the follicle and that these follicles rupture, release their ova and are converted into corpora lutea all within the space of from twenty-four to thirty-six hours. The majority of recent ovulations were found in women between the fifth and the thirteenth day, and between the seventeenth and the twenty-fifth day of their cycles. In some of these women it was impossible to date the cycle. In three women who had metrorrhagia and no definite menstrual rhythm, ovulations were present in all. This fact is of importance in that it may point the way to a clinical use for this substance. However, ovulation did not occur in three women in whom the endometrium showed typical glandular hyperplasia. Clinically, this gonadotropic hormone should prove efficacious in the therapy of patients in whom follicular growth and ovulation are at fault.

Streptococcus in Trichomonas Vaginitis.—Hibbert and Falls list three possible explanations of the clinical observations made so far by investigators studying *Trichomonas vaginalis* vaginitis: (1) an independent causative agent other than the trichomonad, (2) the symbiotic relationship between the trichomonad and the streptococcus as the causative factor and (3) the possibility that the failure of patients harboring the parasite to exhibit clinical manifestations of vaginitis may be due to individual immunity established for one or both of these organisms. The authors deal chiefly with the first of these possibilities. The established pathogenicity of *Streptococcus subacidus* was proved in their work by experimental inoculation of five patients with a pure culture of the organism. Definite pathologic changes were produced in the vagina in four, while in the fifth patient vaginitis was not observed. Objectively the symptoms produced were intense redness of the cervix, vaginal mucosa and vulva, and a gray-white, sticky discharge. Subjectively the patients all complained of a tenderness, burning and itching about the vaginal orifice and a whitish discharge. The symptoms were allowed to remain untreated for from three to four weeks. The treatment instituted was as follows: At no time was any bactericidal agent applied to the vagina; the vaginal tract was first cleansed of accumulated debris with cotton. Then a sterile cotton tampon saturated with a broth filtrate of *Streptococcus subacidus* was packed against the cervix and allowed to remain in place for twenty-four hours before removal by the patient. An intradermal injection of a standardized vaccine made from *Streptococcus subacidus* was also given at this time. The interval between treatments was one week, and the treatments were discontinued during menstruation. All four of these patients were successfully treated and rendered symptom free in from four to seven treatments. The patients have been absolutely free of symptoms for from three to six months. The authors were able to fulfil Koch's postulates: (1) the successful inoculation of a normal patient with a pure strain of a known organism, (2) the reproduction of the characteristic pathologic condition in the host, (3) the recovery and reidentification of the organism from the lesion produced, (4) the successful treatment of the patient by the use of a vaccine made from that organism and the local use of the broth filtrate and (5) the definite demonstration that a specific antibody was produced against the organism introduced. Further efforts to eradicate this streptococcus from the genital tract and to raise the general immunity to this organism seem the logical way to attempt the control of this infestation.

Comparison of Young and Old Primiparas.—Galloway and Paul discuss two groups of primiparas (288 more than 35 and 300 less than 25 years of age) delivered by the same physicians in a private hospital. They find that the average length of labor is increased in the older primiparas but that the duration of labor is of little importance. Toxemia increases with age. The incidence of cesarean section increases likewise probably because of fear and because more of the risk is put on the mother and less on the baby, in order to assure a living child and what, in many cases, will be that family's only off-

spring. It increases also because malpresentations and toxemia increase. The incidence of prematurity increases with age and this factor alone might account for the increase in fetal mortality; because when the gross fetal mortality is broken down into unavoidable and obstetric the increase is found in the unavoidable group. Malpresentations increase, and in turn the added number of these leads to an increase in operative delivery. Why there should be more posterior cephalics, more breech presentations and other odd positions of the fetus among older primiparas it is not possible to state. There were no maternal deaths among the 300 primiparas less than 25 years of age, but three deaths occurred in the primiparas of 35 years or more. All three of the mothers who died were delivered by cesarean section. There were nineteen women among the elderly primiparas in whom the presence of fibroids was a complicating factor, whereas among the 300 young primiparas there were no such cases. Among these nineteen cases there were eleven cesarean sections. Myomectomy at the time of cesarean section is inadvisable, owing to the profuse hemorrhage that generally occurs. Subsequent myomectomy is safer. Only twenty-five of the fifty-one patients delivering for the first time at the age of 40 or more could be traced. Twenty of these stated that both mother and offspring were well. One mother said that her baby, now 13 years of age, had been an invalid since birth by cesarean section; the nature of the invalidism was not stated. One mother refused to give any particulars about her welfare or that of her baby. Cancer developed in three mothers, and two of these had already died.

American Journal of Surgery, New York

41: 369-568 (Sept.) 1938

- Supravaginal Hysterectomy: Review of 535 Consecutive Personal Cases. W. T. Dannreuther, New York.—p. 373.
- *Intradermal Chancroid Bacillary Antigen Test as an Aid in Differential Diagnosis of the Venereal Bubo. R. B. Greenblatt and E. S. Sanderson, Augusta, Ga.—p. 384.
- Rhythmic Surgery. W. H. Lawrence and C. H. Berry, Summit, N. J.—p. 393.
- Effect of Ether and Sodium Amytal Anesthesia on the Blood. F. W. Scurlis, Rochester, Minn.—p. 399.
- Report on New and Effective Cast Material. T. H. Peterson, Boston.—p. 405.
- Miller-Abbott Double Lumen Tube in Intestinal Obstruction: Preliminary Report. R. A. Wise, New York.—p. 412.
- Effect of Perforation on Peptic Ulcer Results. E. L. Eliason and G. M. Thigpen, Philadelphia.—p. 419.
- Perforated Peptic Ulcer: Analysis of 100 Cases. L. S. Fallis, Detroit.—p. 427.
- Surgery of Rectal Diseases by Electrothermic Methods: Based on 1,100 Cases. D. Warshaw, New York.—p. 437.
- Urinary Antiseptics, with Special Reference to Clinical Study of Benzochrone. A. Decker and M. Texon, New York.—p. 449.
- Heart Disease in Pregnancy: Obstetric Aspects. T. R. Turino and A. T. Antony, Brooklyn.—p. 453.
- Advances in Rapid Tissue Section Methods: Evaluation of More Recently Developed Technics. W. E. B. Hall, St. Joseph, Mo.—p. 458.
- Experimental Investigation of Evisceration. I. Kross, New York.—p. 462.

Test for Diagnosis of Venereal Bubo.—Greenblatt and Sanderson produced experimentally a typical textbook picture of chancroid disease in all its phases in a human being by the injection of Ducrey bacilli into the preputial fold. The organism used for this experiment was isolated in pure culture from a chancroidal bubo and maintained in the laboratory for ten months. Two additional observations which should serve to dispel the widespread doubts as to a specific causal organism in what is clinically known as soft sore or chancroid are (1) the reisolation in pure culture, by separation, of the Ducrey bacillus from the secondary lesions and (2) the fact that pus aspirated from the experimental bubo had specific antigenic qualities in that positive cutaneous tests were evoked in known cases of chancroid infection. *Haemophilus ducreyi* can be cultivated with moderate success by growing it beneath the surface of whole defibrinated human blood. The bacillary antigen prepared from such cultures is preferable to bubo pus antigen for a diagnostic cutaneous test. The former gives consistently stronger and more clearcut reactions than the latter. The antigenic quality of chancroid bubo pus is variable, while that of bacillary antigen is constant. The chancroid bacillary antigen as prepared by the authors gave reactions identical to those of dmicos vaccine. The intradermal chancroid bacillary antigen test is an aid in the

differential diagnosis of genital lesions. The buboes of syphilis, gonorrhea, chancroid and venereal lymphogranuloma as well as the pseudobubo of venereal granuloma frequently simulate one another. A positive intradermal chaneroid test commits one to the diagnosis only when the Frei tests, Wassermann reactions, biopsies or smears for venereal granuloma and the like are negative. A repeatedly negative test is of diagnostic value in that it rules out chancroid disease. The various venereal diseases may occur simultaneously in any combination or permutation. A positive chancroid cutaneous test, therefore, in the presence of a positive Frei test, is only presumptive evidence and can be interpreted as diagnostic only when supported by other laboratory evidence such as the cultivation of the Ducey bacillus.

Anatomical Record, Philadelphia

71: 375-512 (Aug.) 1938. Partial Index

- Anatomic Study of Role of Long Thoracic Nerve and Related Scapular Bursae in Pathogenesis of Local Paralysis of Serratus Anterior Muscle. M. T. Horwitz and L. M. Tocantins, Philadelphia.—p. 375.
Afferent Innervation of Skin. A. Kuntz and J. W. Hamilton, St. Louis.—p. 387.
Fascial Continuities in Abdominal, Perineal and Femoral Regions. C. B. McVay and B. J. Anson, Chicago.—p. 401.
Influence of Normal Ovary on Formation of Typical Irradiation Tissues in X-Rayed Ovary. Ida Genther Schmidt, Cincinnati.—p. 409.

Annals of Internal Medicine, Lancaster, Pa.

12: 147-284 (Aug.) 1938

- Consideration of Acquired Resistance of Fixed Tissue Cells to Injury. W. deB. MacNider, Chapel Hill, N. C.—p. 147.
*Prognosis and Treatment of Erysipelas. J. A. Toomey, Lakewood, Ohio.—p. 166.
The Problem of the Development of Hypersensitiveness in Man. F. A. Simon, Louisville, Ky.—p. 178.
Electropyrexia: Technic of Application and Therapeutic Indications. S. L. Osborne and D. E. Markson, Chicago.—p. 189.
Pathology and Mechanism of Anaphylaxis. V. H. Moon, Philadelphia.—p. 205.
Experiences in Treating Toxic Goiter in a Large Public Hospital. W. O. Thompson, S. G. Taylor 3d, K. A. Meyer and R. W. McNealy, Chicago.—p. 217.
*Treatment of Undulant Fever: Report of Five Cases Treated with Specific Polyvalent Serum. H. F. Flippin, Philadelphia.—p. 232.
Determination of Normal Circulation Time from Antecubital Veins to Pulmonary Capillaries by a New Technic. S. Candel, Brooklyn.—p. 236.
Value of Sulfanilamide in Treatment of Infections of Bladder and Upper Urinary Tract: Report of Study of Twenty-Five Patients. W. J. Ezickson, Philadelphia.—p. 244.
A Broader View of Postmortem Examinations. A. Gregg, New York.—p. 249.

Erysipelas.—Toomey studied the records of the patients having erysipelas who died at the Cleveland City Hospital from 1925 to 1937. It was found that those who died were (1) infants less than 1 year of age, especially those with vulval or abdominal erysipelas, (2) patients more than 50 years of age, (3) patients with pulmonary disease such as tuberculosis, bronchopneumonia and lobar pneumonia, (4) patients with chronic organic disease such as chronic myocarditis, valvulitis or arteriosclerotic disease, (5) patients with concomitant acute infections such as influenza and other infectious or contagious diseases, (6) patients who had a severe debilitating illness immediately before the attack of erysipelas, (7) patients with acute or chronic alcoholism and (8) patients who had suffered some injury. Not all patients in these groups died, but all of the patients who died belonged to one of these groups. Only two patients died simply from erysipelas. They were both obese women with questionable pulmonary involvement. Those who were not in these categories recovered, regardless of how many attacks of erysipelas they had had, how often the lesions had spread or what kind of therapy was used. The value of any remedy for erysipelas should be gaged by its ability to save the patients who fall in those groups who usually die; the other patients get better anyway. The benefits that result from the use of newly discovered therapies are sometimes so obvious that control cases seem unnecessary. This is not true of erysipelas antitoxin, but with sulfanilamide in the treatment of erysipelas it is true. With antitoxin the results were questionable save in infants. Seventy-two of seventy-six patients treated with sulfanilamide have recovered and three have died, a mortality rate of 4 per cent. With the use of sulfanilamide the lesions of erysipelas become dusky red and purplish within

the first twelve to twenty-four hours and disappear completely within four to ten days. The inflammatory reaction is likewise gone and the patient is subjectively better within twelve to twenty-four hours. No patient has had massive local desquamation following this treatment. The temperature comes down in a few days and usually by lysis. The lesion spread in only two cases. The author concludes that, if the experience at the Cleveland City Hospital is the general experience, sulfanilamide will become the drug of choice in the treatment of erysipelas. In cases of hepatitis or sensitivity to sulfanilamide, antitoxin should be tried. An effort should be made to institute treatment early.

Treatment of Undulant Fever.—Flippin used a sterile polyvalent antimelittensis serum of bovine origin with preservative in the treatment of five proved cases of undulant fever. Two separate groups of cattle were used in the production of the antiserum. One group received, intravenously, ascending doses of heat killed suspensions of *Brucella abortus*. The other group received heat killed suspensions of *Brucella melitensis*. The series of injections (three per week) necessary to produce an agglutinin titer of 1:1,600 or more against the specific antigen required approximately two months of such treatment. Serums of individual bleedings from each group having sufficient potency, to which 0.35 per cent phenol had been added as a preservative, were pooled and allowed to age. Equal parts of *Brucella abortus* antisera and *Brucella melitensis* antisera were mixed and filtered. The final mixture had an agglutinin titer of 1:800 against both *Brucella abortus* and *Brucella melitensis*. The treatment varied at first, but now the author believes the method of choice is an initial intramuscular injection of 1 cc. of serum as a test dose followed in twenty-four hours, if no reaction occurs, by six daily intravenous injections of 50 cc. of serum. The serum is best given with 100 cc. of physiologic solution of sodium chloride over a period of fifteen minutes. The duration of the patient's illness varied from one to thirteen months. At the present time all five patients are in good health, with apparent cures ranging in duration from eight to twenty-four months.

Annals of Surgery, Philadelphia

108: 321-480 (Sept.) 1938

- Gelatinous Mammary Cancer. C. F. Geschickter, Baltimore.—p. 321.
*Differential Diagnosis of Hyperparathyroidism, with Special Reference to Polyostotic Fibrous Dysplasia (Lichtenstein—Jaffe). J. H. Garlock, New York.—p. 347.
*Treatment of Postoperative Tetany with Dihydratachysterol. O. C. Pickhardt and A. Bernhard, New York.—p. 362.
Congenital Diaphragmatic Hernia. E. J. Donovan, New York.—p. 374.
Direct Inguinal Hernia: Presentation of Operation for Its Cure. C. R. Robins, Richmond, Va.—p. 389.
Madelung's Deformity. J. I. Anton, G. B. Reitz and M. B. Spiegel, Brooklyn.—p. 411.
Intra capsular Fractures of Neck of Femur: Study of 190 Cases. P. A. Wade, New York.—p. 440.

Hyperparathyroidism.—Garlock suggests that the surgeon, when confronted with suspicious osseous lesions evident in the roentgenograms and serum estimations of calcium and phosphorus which are outside the normal limits and in spite of the fact that calcium metabolic studies may show a negative balance, should not be too hasty to advise exploration of the neck for a parathyroid adenoma. When doubt exists as to the diagnosis, additional investigation should be undertaken to clarify the situation. This consists of x-ray examination of the skeleton to determine whether the osseous lesions have a predominantly unilateral distribution and the biopsy of the bone in question. The latter will definitely establish the diagnosis by differentiating the characteristic histologic pictures of polyostotic fibrous dysplasia and hyperparathyroidism.

Dihydratachysterol in Postoperative Tetany.—Pickhardt and Bernhard report their experience with a 0.5 per cent sesame oil solution of dihydratachysterol in the treatment of five cases of tetany following surgery on the thyroid. The conclusion is that dihydratachysterol has great value in the control of postoperative tetany. The symptoms of tetany can be alleviated within forty-eight to seventy-two hours after treatment has been instituted. Therapy with dihydratachysterol must be strictly individualized, i. e. the blood calcium level must be carefully checked at intervals before and after

medication has been instituted. Until the maintenance dosage has been determined, the amount of dihydrotachysterol given by mouth may vary from 1 to 3 cc. every other day to 1 to 2 cc. weekly, depending on the severity of the deficiency. The authors have on occasion administered dosages as high as 10 cc. daily for a period of several days, but during this period the patient's serum calcium was checked carefully. The product is not harmless, and excessive dosage may well induce symptoms of hypercalcemia. A plea is made for the routine determination of serum calcium both preoperatively and postoperatively in all thyroidectomies. The authors found this new substance of definite value from both a subjective and an objective standpoint in the control of tetany. These observations, taken in conjunction with those of Holtz and his co-workers, would suggest that dihydrotachysterol merits further chemical study and it is recommended for the treatment of postoperative hypoparathyroid tetany.

Archives of Internal Medicine, Chicago

G2: 355-546 (Sept.) 1938

- *Lipoid Nephrosis: Study of Nine Patients, with Special Reference to Those Observed Over a Long Period. F. D. Murphy, L. M. Warfield, J. Grill and E. R. Annis, Milwaukee.—p. 355.
- Thrombo-Endocarditis in Rabbits: New Disease Due to an Infraviruses (?). G. Andrei and P. Ravenna, Turin, Italy; translated by R. Kemel, Chicago.—p. 377.
- *Pneumococcal Endocarditis. J. M. Rueggsegger, Cincinnati.—p. 388.
- Primary Benign Tumor of the Heart of Forty-Three Years' Duration. S. Strouse, Los Angeles.—p. 401.
- Wood in Thrombo-Angiitis Obliterans. Grace M. Roth, Elizabeth V. MacLay and E. V. Allen, Rochester, Minn.—p. 413.
- Bilateral Cortical Necrosis of the Kidneys: Report of Three Cases. C. F. Garvin and N. Van Wessel, Cleveland.—p. 423.
- Insulin Resistance: Report of Case of Marked Insensitiveness of Long Duration Without Demonstrable Cause. A. Marble, Boston.—p. 432.
- Protamine Zinc Insulin: Clinical Observations and Comparative Analysis of Blood Sugar Curves Obtained with Use of Protamine Zinc Insulin and with Regular Insulin. F. Neuhoof and S. Rabinovitch, St. Louis.—p. 447.
- Diffuse Arterial Disease with Hypertension: Two Unusual Cases of Contrasting Types. E. F. Rosenberg, N. M. Keith and H. P. Wagener, Rochester, Minn.—p. 461.
- Vascular Diseases: Review of Some of the Recent Literature, with a Critical Review of the Surgical Treatment. G. W. Scupham, G. de Takáts, T. R. Van Dellen and W. C. Beck, Chicago.—p. 482.

Lipoid Nephrosis.—Murphy and his co-workers report their nine cases of lipoid nephrosis in order to (1) show by histologic and prolonged clinical study that lipoid nephrosis is different from chronic glomerulonephritis with the nephrotic syndrome and that there is justification on clinical grounds alone for this distinction, (2) establish lipoid nephrosis as a clinical and pathologic entity, (3) show that patients with lipoid nephrosis recover while those with chronic glomerulonephritis usually do not and (4) present a clinical study with prolonged observations and histologic examinations which may help to clarify some aspects of the controversy and may help to establish the individuality of lipoid nephrosis. Two patients died and were studied after death, six recovered completely and one is still under observation. The period of study of these patients varied from three months to fifteen years. Most patients were observed longer than seven years. The histologic examination of the kidneys of the two patients who died failed to show evidences of chronic glomerulonephritis. Degenerative changes characteristically described as features of lipoid nephrosis were present. In one case the special staining methods of Bell were used, and not even thickening of the basement membrane of the capillaries was observed. A satisfactory explanation is lacking for the hyperpermeability of the capillaries of the glomeruli. The present report tends to support the view that there is justification for the distinction between lipoid nephrosis and chronic glomerulonephritis. The authors believe that there are ample grounds for this because of the favorable prognosis in lipoid nephrosis as contrasted with the poor one in chronic nephritis. Although lipoid nephrosis is a rare disease compared with chronic nephritis, there is sufficient reason for maintaining the distinction of lipoid nephrosis in the classification of Bright's disease.

Pneumococcal Endocarditis.—During a period of twenty-three months 655 patients were admitted to the medical service of the Cincinnati General Hospital with acute pneumococcal infection, in nineteen of whom the diagnosis of acute endo-

carditis was made, either clinically or by pathologic and bacteriologic methods, giving an incidence of 2.9 per cent. Seventeen of the patients were observed by Rueggsegger. In the literature the incidence has been reported as varying from 0.06 to 2 per cent. Whenever clinical and necropsy incidences are recorded the impression is that pneumococcal endocarditis is considerably more common than is usually supposed. A consideration of the relative frequency of the etiologic agents of bacterial endocarditis tends also to show that the importance of the pneumococcus may have been underestimated. During the same twenty-three months forty-six necropsies revealed acute or subacute vegetations on one or more valves, and in fifteen cases the vegetations were proved to be due to the pneumococcus. Preexisting disease of the valvular endocardium apparently has little influence as a predetermining factor in pneumococcal endocarditis. In the nineteen patients, valvular incompetence due to an antecedent infection was diagnosed only once, although two other patients had a history of rheumatic symptoms. Four of the patients had serologic evidence of syphilis, but none had signs of syphilitic aortitis or valvulitis. The endocarditis followed frank lobar pneumonia in fifteen patients while under observation, or there was a history typical of that disease. Pneumococcal endocarditis usually occurs as a complication or sequela of pneumococcal pneumonia, runs an acute course, attacks especially the valves of the left side of the heart, is characterized by embolic phenomena and terminates in the majority of instances in purulent meningitis. As serum and chemotherapy of pneumococcal endocarditis has been almost uniformly unsuccessful, therapy should be largely prophylactic; the prevention of bacteremia by means of potent specific serum and the removal or drainage of purulent foci.

Arkansas Medical Society Journal, Fort Smith

35: 69-88 (Sept.) 1938

- Symptoms, Diagnosis and Treatment of Cancer of Stomach. J. S. Horsley, Richmond, Va.—p. 69.
- Factors Relating to Treatment of Cervix Uteri. G. H. Johnson, Little Rock.—p. 74.
- The Doctor and the Dollar. R. L. Woolsey, Fort Smith.—p. 77.

Canadian Medical Association Journal, Montreal

39: 207-312 (Sept.) 1938

- *Esophageal Hiatus Hernia, with Special Reference to Its X-Ray Diagnosis. D. Eisen, Toronto.—p. 207.
- Diverticulum of the Duodenum. D. Wheeler, Winnipeg, Man.—p. 214.
- Unusual Injuries of the Tarsus. G. A. Fleet and F. D. Ackman, Montreal.—p. 219.
- Clinical Importance of Accessory Spleens: Report of Case. R. F. Robertson, Montreal.—p. 222.
- Identical Dupuytren's Contracture in Identical Twins. H. Couch, Toronto.—p. 225.
- *Physiologic Studies in Experimental Drowning: Preliminary Report. F. G. Banting, G. E. Hall, J. M. Janes, B. Leibel and D. W. Loosheed, Toronto.—p. 226.
- Insulin Shock Treatment of Schizophrenia. N. L. Easton, New Toronto.—p. 229.
- Tonsillectomy Under Intravenous Anesthesia in Children Suffering from Chronic Respiratory Diseases. K. Hutchison, H. S. Mitchell and H. McHugh, Montreal.—p. 237.
- Successful Excision of a Tumor of the Pineal Gland. D. W. Pratt and E. F. Brooks, Toronto.—p. 240.
- Diagnosis of Cholelithic Disease. A. R. Munroe and M. M. Serebo, Edmonton, Alta.—p. 244.
- Pick's Disease (Mediastinopericarditic Pseudocirrhosis of the Liver): Case, with Pericardial Resection and Recovery. G. F. Strong, Vancouver, B. C.—p. 247.
- Perfecting of Anesthesia. W. Bourne, Montreal.—p. 249.
- Illness Other Than Diabetic Complications in Insulin Patients. A. F. Van Wart, Fredericton, N. B.—p. 253.
- Facts, Fads and Fancies in Treatment of Acne Vulgaris. L. P. Erezau, Montreal.—p. 257.
- Skin Diseases in Children. H. A. Dixon, Toronto.—p. 261.

Esophageal Hiatus Hernia.—Diaphragmatic hernia and the esophageal hiatus type in particular offers an example of a disease the study and elaboration of which is dependent on the use of the x-rays. Eisen divides these hernias into three anatomic types: short esophagus, para-esophageal and gastro-esophageal types. The condition is now regarded as comparatively common. Examination of several large series of published cases reveals a preponderance of females, the ratio to males being about 2:1. In the authors' thirty-three cases there were twenty-two females. Since abdominal distention plays an undoubted part in the etiology of this condition, this

predominant female incidence might be explained by multiple pregnancies and the greater tendency to constipation and adiposity in the female. When the bodily habitus is mentioned, it appears that the condition is more common in the stocky or sthenic types. The average age of the patients was 53 years, the youngest 25 and the oldest 78. The thirty-three cases were encountered in the course of a routine gastrointestinal x-ray examination of 1,138 patients. The size of the hernia varied from that of a cherry to that of an orange. The condition may be incidental and symptomless, or it may simulate a chronic cholecystitis or a peptic ulcer. Less commonly there may be dysphagia or anginoid symptoms. All symptoms are worse after a heavy meal and on lying down and are relieved on standing or vomiting. There are no characteristic physical signs. Roentgenologically, a characteristic protrusion of the fundus of the stomach is seen above the diaphragm. Roentgenologically the condition must be differentiated from ampullary dilatation of the lower end of the esophagus, cardiospasm, ulcer of the esophagus and peptic esophagitis, cardio-esophageal relaxation, cancer and diverticulum of the lower end of the esophagus, a diverticulum of the stomach and hour-glass stomach. Medical treatment is largely symptomatic and usually satisfactory. Surgery is indicated in cases in which the symptoms are severe and do not respond to medical treatment. The short esophageal type is not amenable to surgery. Recurrences are not uncommon.

Experimental Drowning.—Banting and his co-workers discuss some of the physiologic mechanisms that they observed in experimental drowning. The condition is essentially one of asphyxia. There are two types of drowning. In type 1 there is a period of apnea during which time there occurs an initial struggle followed by a cessation of movement and then swallowing takes place. When the stomach is distended a period of spasmodic convulsions intervenes, followed by vomiting. This period of apnea is replaced by an interval during which from two to ten gasps occur. Reflexes then disappear and somatic activity apparently ceases. In type 2 drowning the sequence of events in the apneic stage is practically the same as in type 1 but is not followed by gasping. Consequently little if any water enters the lung and death is due to obstructive asphyxia. The cardiac rate and blood pressure present terminally distinctive differences in the two types. In type 1 the pressure falls suddenly just before death to approximately zero; the cardiac rate likewise decreases suddenly, fibrillation frequently occurs and electrocardiographic activity ceases within one to two minutes. In type 2 the blood pressure falls more gradually, the cardiac rate decreases to from ten to fifteen beats per minute and later the ventricular complexes disappear. The auricular complexes may be present for from thirty to forty-five minutes after death. The necropsy in experimental drowning shows the lungs to be hemorrhagic and edematous. In both types of drowning edematous fluid and froth is found throughout the bronchial tree and exudes freely from the cut surface of the lung. Much more fluid and froth are found in type 1 than in type 2 drowning. A variable amount of water is found in the lungs, depending on the number of gasps. If dyed water is used and the lungs are examined immediately after death, irregularly stained areas, extending out to the periphery of the lung, are seen adjacent to tissue which appears unstained and relatively normal. Microscopically the tissue resembles that found in acute pulmonary edema. Invariably the right side of the heart is found to be greatly distended, the left contracted and empty. From the experimental results obtained the following resuscitation measures are recommended: As soon as a person is recovered from the water he should be held up so that water may drain from the stomach and lungs and then placed in the prone position. All foreign matter should be removed from the mouth and larynx, the tongue pulled forward and the Schafer method of artificial respiration immediately started. If a free passage of air in and out of the chest cannot be detected, the larynx should be swabbed with 10 per cent cocaine or a catheter passed into the trachea. Insufflation of 20 per cent carbon dioxide and 80 per cent oxygen has been found to be most effective, delivered at 3

liters per minute into the trachea. If intubation has not been done this gas mixture may be delivered through a nasal catheter into the pharynx. In type 2 drowning it is suggested that a pearl of amyl nitrite blown in through a tracheal catheter before insufflation is begun is most effective. Epinephrine 40 minims (2.5 cc.) of 1:1,000 has been found to be indicated to assist the cardiac action. Atropine from $\frac{2}{100}$ to $\frac{4}{100}$ grain (0.0013 to 0.0026 Gm.) injected intravenously decreases the froth and edema in the lungs as well as increasing the cardiac rate and removing inhibitory influences of the parasympathetic nervous system. It is highly important to keep the patient warm and to massage the extremities toward the heart.

Georgia Medical Association Journal, Atlanta

27: 295-336 (Aug.) 1938

Hysterectomy: Discussion of Cases. W. G. Elliott, J. C. Patterson and T. S. Gatewood, Cuthbert.—p. 295.

*Use of Atabrine in Treatment and Control of Malaria Among a Group of Industrial and Agricultural Employees in Georgia. C. F. Holton, Savannah, and M. E. Winchester, Brunswick.—p. 299.

Diagnostic Traps in Gastro-Enterology. T. Johnson, Atlanta.—p. 304.

Is the Death Rate from Heart Disease Increasing? S. T. R. Revell, Louisville.—p. 309.

Vesicular Eruptions of the Hands: Report of Cases. P. H. Nippert, Atlanta.—p. 313.

Toxic Exanthema Following Prolonged Atabrine Administration and Resembling Brill's Typhus Fever: Report of Case. W. E. Storey, Columbus.—p. 317.

Present Day Concepts in the Treatment of Malaria. R. A. Hill, Thomasville.—p. 318.

Intracutaneous Test for Chancroidal Infection: Comparison of Antigens: Part II. R. B. Greenblatt and E. S. Sanderson, Augusta.—p. 320.

Nicotinic Acid in Prevention and Treatment of Pellagra. V. P. Sydenstricker, Augusta.—p. 321.

Atabrine in Control of Malaria.—On Jan. 4, 1937, Holton and Winchester made a survey of 1,848 industrial and agricultural workers and prepared thick blood smears. All blood smears throughout the period were examined by the state health department of Georgia. Every person, regardless of the presence or absence of parasites in the blood, was given 0.3 Gm. of atabrine daily for five days. The atabrine was administered personally by trained public health nurses so that no error could occur from irregularity of treatment. Two weeks later a second survey was made during which 1,102 blood smears were examined. All persons who had had positive blood smears on the first examination were included in the second examination. All persons with positive blood smears at the second examination were given 0.02 Gm. of plasmochin daily for three days. On March 22 a third blood smear was taken of all persons who had had positive results in the blood at the beginning of the experiment. The total parasite index for all ages decreased from 8.5 to 2.9 per cent after the first course of atabrine. The third reexamination of the 157 individuals whose smears were originally positive showed two positives, both in the adult group, one of which had been diagnosed *Plasmodium falciparum* infection previously, but which was probably a mixed infection of *Plasmodium vivax* and *Plasmodium falciparum*. This blood now showed only *Plasmodium vivax* parasites. The second patient had *Plasmodium falciparum* parasites at both examinations. In no case throughout the entire experiment did clinical symptoms of malaria appear after a single course of atabrine or plasmochin. The single five day course of atabrine accomplished a parasitic cure in 90 per cent of *Plasmodium vivax* infections and in 79 per cent of *Plasmodium falciparum* infections. After the additional three day course of plasmochin to the patients not parasitically cured by atabrine, all those infected with *Plasmodium vivax* and 99 per cent of those infected with *Plasmodium falciparum* were free from parasites.

Iowa State Medical Society Journal, Des Moines

28: 421-472 (Sept.) 1938

Urinary Antisepsis. E. N. Cook, Rochester, Minn.—p. 421.

Tumors of the Spinal Cord: Some Clinical Considerations Recoverability of Cord Function. O. R. Hyndman and E. P. Russell, Iowa City.—p. 425.

The Undernourished Child. R. Stahr, Fort Dodge.—p. 435.

Cardiovascular Syphilis. R. J. Harrington, Sioux City.—p. 438.

Depressive States in General Practice. J. I. Marker, Davenport.—p. 443.

Diverticulitis and Diverticulosis of the Colon. C. A. Trueblood, Indianola.—p. 447.

Journal of Immunology, Baltimore

35: 75-154 (Aug.) 1938

- Group Specific Agglutinins in Rabbit Serums for Human Cells: IV. Immune Group Specific β Agglutinins. Shirley Battey, C. A. Stuart and K. M. Wheeler, Providence, R. I.—p. 75.
- Incidence of Agglutinins for Paratyphenteric Bacilli in Serums from Human Beings and from Animals. H. J. Sears, Lillian Schwichtenberg and Marian Schwichtenberg, Portland, Ore.—p. 83.
- Quantitative Studies of Reaction of Complement Fixation with Tuberculous Immune Serum and Antigen. A. Wadsworth, F. Maltaner and Elizabeth Maltaner, Albany, N. Y.—p. 93.
- Quantitative Studies of Reaction of Complement Fixation with Syphilitic Serum and Tissue Extract. A. Wadsworth, F. Maltaner and Elizabeth Maltaner, Albany, N. Y.—p. 105.
- Rapid Method for Standardization of Antimeningococcus Horse Serum Type I. P. A. Little, Pearl River, N. Y.—p. 117.
- Further Observations on Toxicogenic Properties of Hemolytic Streptococci. Julia M. Coffey, Albany, N. Y.—p. 121.
- Studies of Staphylococcus Toxin: Toxin-Red Cell Reaction. B. S. Levine, Washington, D. C.—p. 131.
- *Study of Strains of Pneumococci Immunologically Closely Related to Both Type XI and Type XVI Pneumococci. M. Finland and J. W. Brown, Boston.—p. 141.

Pneumococci Related to Types XI and XVI.—Finland and Brown studied a number of strains of pneumococci that are immunologically closely related to typical strains of both type XI and XVI pneumococci but that are probably distinct from either of these types. One such strain was previously observed by Wirth and Bander and called "double-type XI-XVI." By tests for agglutination, passive protection in mice, capsular swelling and absorption of agglutinins the strains exhibiting cross agglutinations were shown to be distinct from either type XI or XVI but immunologically related to both.

Journal of Nervous and Mental Disease, New York

88: 273-396 (Sept.) 1938

- Abortion of Recurrent Depressive Psychoses. L. B. Holman, Baltimore.—p. 273.
- Some Clinical Neurologic Findings in Epilepsy: Preliminary Report. S. M. Weingrow, New York; T. S. P. Fitch, Plainfield, N. J., and A. W. Pigott, Skillman, N. J.—p. 281.
- Indexes of Body Build, Their Relation to Personality. S. H. Kraines, Chicago.—p. 309.
- Neuritis of Cranial Nerves. A. T. Stegmann, Cleveland.—p. 316.
- Some Uses of Diallylmalonylurea in Psychiatry: Preliminary Study. G. D. Woodward, Cincinnati.—p. 324.
- Blindness Passed Unobserved for Many Years. W. S. Bab, Berlin, Germany.—p. 327.
- *Prostigmine in Myasthenia Gravis: Report of Two Cases. M. Tarlau, Central Islip, N. Y.—p. 330.

Prostigmine in Myasthenia Gravis.—Tarlau reports two cases of myasthenia gravis in which the use of prostigmine orally elicited a temporary remission of symptoms in one case, although this patient subsequently died, and a complete remission for nine months (to the time of writing) in the other. In the patient who finally died there developed a rapidly increasing tolerance or refractoriness to the drug. This phenomenon was not observed in the other case and has heretofore not been stressed in the literature. Prostigmine was found to be more effective than any other medication used, but the problem of myasthenia gravis is still unsolved and probably will remain so until the etiology is established.

Journal of Nutrition, Philadelphia

16: 103-208 (Aug.) 1938

- Effect of Autoclaving on Nutritive Value of Edestin. H. A. Waisman and C. A. Elvehjem, Madison, Wis.—p. 103.
- Effect of Amino Acid Supplements and of Variations in Temperature and Duration of Heating on Biologic Value of Heated Casein. Ethelyn O. Greaves, Agnes Fay Morgan and Minnette K. Loveen, Berkeley, Calif.—p. 115.
- Biologic Value of Milk and Egg Protein in Young and Mature Rats. Emma E. Sumner, Rochester, N. Y.—p. 129.
- Biologic Value of Milk and Egg Protein in Human Subjects. Emma E. Sumner and J. R. Murlin, Rochester, N. Y.—p. 141.
- Effect of Various Fractions of Liver on Experimental Canine Black-tongue. H. I. Harvey, D. T. Smith, E. L. Persons and Margaret V. Burns, Durham, N. C.—p. 153.
- Comparison of Sodium Fluoride in Drinking Water and Similar Levels of Cryolite in the Diet on the Fluorine Content of the Body. S. Marcovitch and W. W. Stanley, Knoxville, Tenn.—p. 173.
- Differentiation of Rat Dermatitis Factor and the Chick Dermatitis Factor from Nicotinic Acid. W. J. Dann, Durham, N. C., and Y. Subbarow, Boston.—p. 183.
- Production of Microcytic Hypochromic Anemia in Puppies on Synthetic Diet Deficient in Rat Antidermatitis Factor (Vitamin B₆). P. J. Fouts, Indianapolis; O. M. Helmer, S. Lepkovsky, Berkeley, Calif., and T. H. Jukes.—p. 197.

Journal of Pediatrics, St. Louis

13: 157-302 (Aug.) 1938

- Subphrenic Abscess in Children, with Special Reference to Roentgen Signs of Transphrenic Infection. W. E. Anspach, Chicago.—p. 157.
- Pneumatosis of Intestine in Infancy. T. W. Botsford and C. Knicker, Boston.—p. 185.
- Significance of Conditions of Exposure in Study of Measles Prophylaxis. Added Criterion in Evaluation of Measles Prophylactic Agents. S. Karelitz, assisted by Ruth F. Karelitz, New York.—p. 195.
- Atelecstasis of Lungs in the Newborn Baby, Resulting from Lesions of Nervous Centers. R. Debré, J. Marie, M. Lamy and de Font-Réaulx, Paris, France.—p. 208.
- *Serum Treatment of Pneumonia in Childhood. Rosa Lee Nemir, New York.—p. 219.
- Myotonia Congenita: Report of Case Treated by Quinine. W. A. Hawke, Toronto.—p. 236.
- Ripe Banana as Complementary Feeding in Infants: Study of 444 Cases. J. D. Craig, New York.—p. 239.
- Treatment of Tuberculosis of Spine by Spinal Fusion: Results in 309 Children Less Than 10 Years of Age. W. E. Swift, New York.—p. 248.

Serum Treatment of Pneumonia in Childhood.—Nemir compares the results of antipneumococcus serum in 151 cases of pneumonia in infants and children with 253 control cases treated over a period of five years. The evidence shows that types I and XIV serums are valuable and effective therapeutic aids. In a few patients types VII, V and II serums were similarly valuable. Even though a dramatic response to serum therapy may be obtained, other considerations are important prior to the decision to use antipneumococcus serum in children. Since the mortality rate of lobar pneumonia is low in children more than 2 or 3 years old, a specific therapeutic agent is not imperative. Pneumococcus serum involves a minimal sensitization to horse serum. Sensitization has not been demonstrable in several cases as shown by cutaneous and ocular tests at a later time. Two patients were treated a second time, one from three to four weeks later, and the other one a year later without any reaction in the first and an accelerated serum sickness in the second. Treatment of patients with serum late in the disease is probably useless in patients less than 12 years old, since it appears to affect mortality only slightly and complications not at all. However, in the presence of a bacteremia, even though discovered late, serums shown to be effective (in types I and XIV, and probably in VII, V and II) are advised. Bacteremia, a rare complication in children, when present indicates severe and overwhelming infection. Most workers with antipneumococcus serum have constantly emphasized the importance of early treatment. Infants severely ill with type XIV pneumococcus pneumonia should receive homologous serum early in the disease, since in this age group (less than 2 years) the mortality rate is high. The use of a combined nonspecific serum in the treatment of a severely ill infant or child before the pneumococcus is typed is not recommended. Serum is effective only for the specific type associated with the disease. Although the efficacy of serum has been demonstrated previously, the author advises its use only for those severely ill patients whose cases are diagnosed early and for young infants, in whom the mortality rate is high. The mortality rate was low in the two groups that he considers and the administration of serum showed no reduction. The incidence of empyema was reduced in patients with types I, XIV and V lobar pneumonia receiving serum early in the disease. A dramatic precipitation of the crisis was observed in the majority of patients treated with specific antibody within twelve to eighteen hours after the first treatment.

Medical Annals of District of Columbia, Washington

7: 241-268 (Aug.) 1938

- Modern Treatment of Syphilis. R. A. Vonderlehr, Washington.—p. 241.
- *Creeping Eruption: Report of Two Cases and Brief Review of Literature. I. L. Sandler, Washington.—p. 245.
- Causes of Neonatal Mortality in the District of Columbia. Marian M. Crane, Washington.—p. 248.
- The Problem of Stillbirths. Ethel C. Dunham, Washington.—p. 252.
- Mental Disorder as Seen in General Practice. J. E. Lind, Washington.—p. 257.

Creeping Eruption.—Creeping eruption is a public health problem. It is probable that many cases are never reported or recognized, and that the condition is more widespread than now considered. Interest of the proper authorities should be

aroused in order to prevent the dissemination of this troublesome infestation at beaches. Sandler deals only with creeping eruption as originally described by Kirby-Smith, Dove and White and caused by the larval stage of the nematode *ancyllostoma braziliense*. The distribution of the eruption in the United States has been confined principally to the coastal plains from New Jersey to Texas, with most of the cases occurring in Florida. Thoroughly freezing the suspected area with ethyl chloride is often effective, or compresses of cotton saturated with ethyl acetate may prove curative. All dogs and cats (including pets) should be denied the privilege of beaches. Tetrachlorethylene is the standard drug for removing hookworm in veterinary practice.

Nebraska State Medical Journal, Lincoln

23: 321-360 (Sept.) 1938

- The Speakers' Bureau of the Committee of Public Health and Medical Education of the Nebraska State Medical Association. J. D. McCarthy, Omaha.—p. 321.
Democracy in Medical Organization. R. H. Whitam, Lincoln.—p. 327.
Responsibilities and Problems of Fifty Years of Practice. M. Nielsen, Blair.—p. 329.
Treatment of Arthritis. F. L. Dunn and E. E. Simmons, Omaha.—p. 330.
Temporomandibular Joint Syndrome. A. F. Tyler, Omaha.—p. 333.
Cancer of the Breast. H. H. Davis, Omaha.—p. 336.
Tubercular Peritonitis. M. Emmert, Omaha.—p. 339.
Diagnosis and Treatment of Ectopic Pregnancy. M. E. Grier, Omaha.—p. 340.
Treatment of Emergencies in Ear, Nose and Throat. H. E. Kully, Omaha.—p. 343.
Insulin Shock Therapy of Schizophrenia. J. C. Nielsen, A. H. Fechner and J. H. Waterman, Ingleside.—p. 345.
Cardiac Clinic Number VII: Cardiac Circulation in Hypertension. J. P. Tollman, Omaha.—p. 348.

New England Journal of Medicine, Boston

219: 251-288 (Aug. 25) 1938

- Congenital Webbing of the Neck. D. W. MacCollum, Boston.—p. 251.
The Problem of Congenital Syphilis in Boston: Two Year Survey of a Clinic. J. A. V. Davies and Margaret H. Walter, Boston.—p. 255.
Accidental Injury to the Heart by Needle Puncture: Report of Four Cases. W. B. Bean, Boston.—p. 257.
Dangers of Tuberculosis in Childhood: Study of Hospital Mortality. C. A. Smith, Boston.—p. 260.
Inionagus: Rare Form of Siamese Twins. J. B. Vernaglia, Medford, Mass.—p. 266.
Use of Prostigmine as Preparation for Abdominal Roentgenography: Preliminary Report. M. J. Farrell, Waltham, Mass.—p. 270.

219: 289-322 (Sept. 1) 1938

- Diagnosis of Causes of Heart Failure. L. Hamman, Baltimore.—p. 289.
Nailing the Fractured Neck of the Femur with the Aid of the Fluoroscope. N. C. Browder, Boston.—p. 296.
*Anal Fissure: Evaluation of Treatment with Oil Injections. G. S. Speare and R. E. Mabrey, Boston.—p. 302.
Spivack Gastrostomy. F. H. Baehr and S. Frehling, Westfield, Mass.—p. 305.

219: 323-366 (Sept. 8) 1938

- Immediate or Deferred Surgery for General Peritonitis Associated with Appendicitis in Adults. I. J. Walker, Boston.—p. 323.
Immediate or Deferred Surgery for General Peritonitis Associated with Appendicitis in Children. W. E. Ladd, Boston.—p. 329.
Treatment of Peritonitis Complicating Appendicitis. A. M. Shipley, Baltimore.—p. 333.
Acute Bowel Obstruction: Its Recognition and Management. O. H. Wangenstein, Minneapolis.—p. 340.
Clinical Evaluation of Some Nonvolatile Anesthetic Drugs. L. F. Sise, Boston.—p. 349.

Anal Fissure.—Speare and Mabrey treated fifty-three patients with anal fissure with oil injection. With the patient in the right Sims position the skin about the anus is prepared as for an operation and 1 per cent procaine hydrochloride is injected subcutaneously through a 26 gage, 4 cm. needle, beginning about 2 cm. from the posterior commissure. This infiltration is carried out fanwise and may be extended into the external sphincter. This injection may be dispensed with, since that of the oil causes only slight discomfort. With the left index finger in the anus as a guide, the solution of oil is injected slowly with a Luer Lok syringe through a 24 or 25 gage needle. Injection is continued as the needle approaches the external sphincter, and the solution is injected into the muscle and under the ulcer. The amount used varies from 1 to 5 cc. The treatment may be repeated at weekly intervals. The authors' patients received from one to four injections. After the injection the patient usually has immediate relief

of pain. Complications must be considered. In two of the patients small abscesses developed at the site of injection one week after treatment. These were opened, with subsequent healing of the fissure. One patient had a pinhead-sized area of cutaneous necrosis. A small superficial fistula developed in another. Two solutions have been used for injection: oil of sweet almonds containing 0.5 per cent nupercaine, 1 per cent phenol and 10 per cent benzyl alcohol and a solution of peach-kernel oil containing 1.5 per cent procaine hydrochloride, 6 per cent butesin and 5 per cent benzyl alcohol. Of the thirty-nine patients treated, 62 per cent were relieved and 38 per cent had recurrences after three months. In comparison, 83 per cent of thirty-five patients were relieved by operation and nine of ten patients gained relief from various kinds of treatment (liquid petrolatum, sitz baths and cauterization with silver nitrate). The main feature in the treatment by the injection of oil is that anesthesia is prolonged with resulting relaxation of the sphincter, pain is relieved and freer drainage is established. Whereas before the injection digital or instrumental examination may be impossible, immediately after the injection it can be performed without pain. The anesthesia lasts from one to three weeks, gradually wearing off. In most cases, especially those patients having simpler fissures without large sentinel piles and underlying pockets, healing takes place before complete sensation returns. The avoidance of a hospital stay, rather than superior results, justifies the use of this method as against operation, which can be performed later if the injections of oil fail.

New York State Journal of Medicine, New York

38: 1103-1150 (Aug. 15) 1938

- Dust and Pulmonary Disease, with Special Reference to Silica Dust. A. J. Vo-wald, Saranac Lake.—p. 1103.
Advanced Cardiovascular Syphilis and Its Management. G. F. Hogan, Brooklyn.—p. 1110.
Early Recognition of Cardiovascular Syphilis. A. Blau, Brooklyn.—p. 1115.
Scientific Glance at Lymphopathia Venereum. H. E. Bacon, Philadelphia.—p. 1123.
Granulosa Cell Tumor of the Ovary. L. H. Meecker and S. A. Localio, New York.—p. 1126.
Combined Nasal Reconstruction and Submucous Resection. J. A. Tamerin, New York.—p. 1129.
Shinle Oil Cancer. R. A. Leonardo, Rochester.—p. 1134.

Public Health Reports, Washington, D. C.

53: 1443-1498 (Aug. 19) 1938

- Endemic Fluorosis and Its Relation to Dental Caries. H. T. Dean.—p. 1443.
Silirosis and Similar Dust Diseases: Medical Aspects and Control. R. R. Sayers and R. R. Jones.—p. 1453.
*Studies on Trichinosis: VII. The Past and Present Status of Trichinosis in the United States and the Indicated Control Measures. M. C. Hall.—p. 1472.

Control Measures in Trichinosis.—According to Hall, the problem of trichinosis in the human being in the United States rests primarily on a basis of swine trichinosis, and swine trichinosis rests primarily on a basis of feeding swine raw or inadequately cooked scraps of pork in garbage, table scraps, swill and the like. The rat plays a minor and not definitely ascertained part in the production of swine trichinosis. The basic solution of the problem is keeping raw and inadequately cooked scraps of pork out of the feed of swine. The control measures invoked in the last fifty years have not visibly lowered the incidence of trichinae in man and swine. The control of trichinosis calls for improvements in methods of raising swine, and these improvements should be specified by the packers as requisites to be met by swine growers before swine can be purchased for marketing as pork and without the need for specific measures to destroy trichinae that may be present in the pork. Packers and swine growers can play a big part in controlling trichinosis, eliminating that hazard to the public health and protecting the swine industry and the packing industry from repercussions that may be expected in the next few years as a result of increased interest in trichinosis. Useless publicity and ill considered legislation are not the correct control measures for trichinosis. The packer and the swine grower should be called in as cooperators in the control of trichinosis. A campaign, coordinated by the United States Public Health Service and the Federal Bureau of Animal

Industry, should be carried out by state, county and city public health and livestock sanitary officers to eliminate the practice of feeding raw and undercooked scraps of pork to swine, and nationwide inspection of meat by professional and trained personnel should be established.

53: 1499-1558 (Aug. 26) 1938

Flora and Fauna of Surface Waters Polluted by Acid Mine Drainage. J. B. Lackey.—p. 1499.

*Studies on Chronic Brucellosis: IV. Evaluation of Diagnostic Laboratory Tests. Alice C. Evans, F. H. Robinson and Leona Baumgartner.—p. 1507.

Comparative Study of Two Strains of Rocky Mountain Spotted Fever Virus, with Special Reference to Weil-Felix Reaction. G. E. Davis and R. R. Parker.—p. 1525.

53: 1559-1592 (Sept. 2) 1938

Frequency of Disabling Illness Among Industrial Employees During 1932-1937 and the First Quarter of 1938. W. M. Gafaer and Elizabeth S. Frasier.—p. 1562.

Changes in Types of Visual Refractive Errors of Children: Statistical Study. A. Ciocco.—p. 1571.

Diagnostic Tests for Brucellosis.—In an effort to determine the value of the various tests for diagnosing undulant fever, Evans and her associates studied six groups of patients (fourteen cases of brucellosis in the past, four of acute brucellosis, twenty-eight of chronic brucellosis, forty-one of possible chronic brucellosis, 321 subjects ill with many other diseases and with no history suggesting brucellosis in the past and twenty-eight healthy subjects). Data on one or another of the specific tests are lacking in only sixty-one cases. No single test (other than the isolation of the *Brucella* organism from the patient) can be relied on to determine *Brucella* infection in any given case. An agglutinin titer of 1:40 was found to be the minimum suggestive of brucellosis. Forty-six per cent of the twenty-eight cases of chronic brucellosis gave a negative agglutination reaction and four of the seven cases from which *Brucella* was cultivated gave a negative agglutination reaction; therefore a negative agglutination reaction cannot be regarded as evidence against infection. On the other hand, a positive agglutination reaction is evidence of infection. An agglutinin titer of 1:40 or higher occurred about eleven times as frequently in chronic brucellosis as in other diseases. The higher the titer, the greater is its significance. A positive cutaneous reaction occurred more than four times as frequently in cases of chronic brucellosis as in other diseases. It may therefore be regarded as suggestive of infection, though it is less reliable than a positive agglutination reaction. The opsonocytaphagic reaction was found to be the least reliable of the specific tests, because positive reactions are not uncommon in other diseases. A positive opsonocytaphagic reaction occurred about twice as frequently in chronic brucellosis as in other diseases. Positive opsonocytaphagic and cutaneous reactions add weight to the evidence given by a positive agglutination reaction. The combination of all three positive reactions occurred about ten times as frequently in chronic brucellosis as in other diseases. However, all three specific tests gave negative results in two cases from which *Brucella* were obtained.

Southern Surgeon, Atlanta, Ga.

7: 285-384 (Aug.) 1938

Cineplastic Amputation. H. H. Kessler, Newark, N. J.—p. 285.
Nonpenetrating Wounds of the Abdomen. J. McLeod, Florence, S. C.—p. 293.

Disease of Gallbladder and Bile Ducts: Symptomatology and Results of Surgical Treatment. A. Street, Vicksburg, Miss.—p. 299.

Protosil and Sulfanilamide in Treatment of Gas Gangrene: Report of Two Cases. G. W. Fuller and J. M. Kellum, Atlanta, Ga.—p. 305.

Modern Methods in Treatment of Pyogenic Infections. C. Lyons, Boston.—p. 308.

Etiologic and Therapeutic Aspects of Bronchiectasis with Clinical Observations on Bronchial Lavage by the Stitt Method. V. K. Hart, Charlotte, N. C.—p. 313.

Diagnosis and Treatment of Lateral Sinus Thrombosis. C. McDougall, Atlanta, Ga.—p. 333.

Importance of Physical Examination in Differential Diagnosis of Chronic Pulmonary Diseases. P. P. Vinson, Richmond, Va.—p. 338.

Development of Various Methods of Ureteral Transplantation and Cystectomy: Addition of Another Method. A. G. Brenizer, Charlotte, N. C.—p. 341.

Surgical Treatment of Hypertension. C. H. Moore, Birmingham, Ala.—p. 353.

Surgery, Gynecology and Obstetrics, Chicago

67: 265-412 (Sept.) 1938

*Conization of the Cervix. N. F. Miller and O. E. Todd, Ann Arbor, Mich.—p. 265.

Tuberculous Peritonitis: Analysis of 257 Cases. J. G. Stubenbord Jr., Douglaston, Long Island, N. Y., and J. Spies, Bombay, India.—p. 273.

Urinary Stress Incontinence: Anatomic Defect Found and a Rational Method for Its Treatment. J. W. Davies, New York.—p. 273.

Clinical and Radiologic Data Associated with Congenital and Acquired Single Kidney. W. F. Braasch and J. W. Merricks, Rochester, Minn.—p. 281.

Investigation of Surgical Anatomy of Ligaments of Knee Joint. M. T. Horowitz, Philadelphia.—p. 287.

*Behavior of Hemoglobin After Blood Transfusion. W. L. Sibley and J. S. Lundy, Rochester, Minn.—p. 293.

X-Ray Diagnosis of Erythroblastosis. L. M. Hellman and F. C. Imig, Boston.—p. 296.

Theca Interna Cone and Its Role in Ovulation. E. O. Strassman, Rochester, Minn.—p. 299.

Etiology of Extra-Uterine Pregnancy. A. J. Osakina-Rojdestvenskii, Leningrad, U. S. S. R.—p. 308.

Surgery of Stomach and Duodenum: Procedures for Peptic Ulcer and Gastric Cancer. E. C. Cutler and R. Zollinger, Boston.—p. 318.

Ankylosis of Temporomandibular Joint. V. H. Kazanjian, Boston.—p. 333.

Injection of Right Stellate Ganglion with Alcohol in Paroxysmal Tachycardia. E. P. Coleman and D. A. Bennett, Canton, Ill.—p. 349.

Simple Fixation Guide for Fractured Hips. D. Sloane, New York.—p. 354.

Fracture of Femoral Neck: Rapid and Accurate Method of Internal Fixation Using a Flanged Metallic Nail. E. A. Dooley, New York.—p. 356.

Conization of Cervix.—Miller and Todd comment on the 899 electrosurgical conizations of the cervix performed at the University of Michigan Hospital during the last four years. The patient is hospitalized for three or four days. When the cutting current is properly combined with coagulation, the operation becomes a bloodless procedure and in this respect is in striking contrast to most cervical amputations, particularly the Sturmdorf operation. It takes about six weeks for complete epithelization to occur following conization. Stricture is prevented by placing an iodoform wick in the cervical canal at the time of operation in all patients except those who are to have a subtotal hysterectomy. This wick is removed on the third day and the patient is discharged with instructions to take a daily cleansing douche and report twice a week for check-up examination. At this time the cervix is painted with an antiseptic, and a sterile sound or a hemostat is passed into the canal. This procedure is repeated at intervals of two weeks until epithelization is complete. The authors believe that conization is indicated in (1) the correction of minor cervical disease and the prevention of remote complications of the cervix, in patients for whom subtotal hysterectomy is planned, (2) the eradication of deep seated, chronic infections of the cervical canal in older women, (3) for any condition of the cervix for which the Sturmdorf operation is indicated, (4) for obtaining adequate biopsy material in cases in which original biopsy material presented cytologic abnormalities strongly suggesting neoplastic change and (5) as a substitute for older methods of trachelorrhaphy in most women, but especially in elderly women. No serious immediate complication occurred in any of the 899 conizations. During the first few days there is little discharge and no discomfort but on the third or fourth day the discharge becomes profuse and is often bloody. Normally this serosanguineous or bloody discharge persists for two weeks, after which it gradually decreases. Vaginal cleansing douches are essential during this period of healing. Ultimate healing with complete epithelization renders the cervix clean and normal in appearance. In a few patients small areas of delayed epithelization are noted. In these, healing may be hastened by the use of the fine nasal tip cautery. As strictures do occur (6.45 per cent positive and 2.51 per cent probable), some of them severe, this warrants care in the selection of patients for conization and careful observation afterward.

Hemoglobin After Blood Transfusion.—Sibley and Lundy found that, in the average case in which 500 cc. of citrated blood was given by transfusion, there was an increase of about 1.5 Gm. per hundred cubic centimeters (about 9 per cent) in the value for hemoglobin of the recipient's blood. This increase occurred at the end of the second day after

transfusion and tended to drop to about 1 Gm. per hundred cubic centimeters (approximately 6 per cent) by the tenth day after transfusion. It appeared that when 500 cc. of citrated blood was given by transfusion an increase in value for hemoglobin of from 2.12 (about 12.72 per cent) to 2.8 Gm. per hundred cubic centimeters (about 16.8 per cent) could be expected in those cases in which reactions to the transfusion did not occur and in which bleeding did not follow transfusion. The amount of the recipient's increase in hemoglobin was directly proportional to the value of his hemoglobin before transfusion. There was definitely less increase (about 50 per cent) in the hemoglobin when a reaction to the transfusion occurred than when a reaction did not occur.

Western J. Surg., Obst. & Gynecology, Portland, Ore.

46: 395-450 (Aug.) 1938

- Tumors of the Lip and Oral Cavity. D. V. Trueblood, Seattle.—p. 395.
- Fracture Involving the Epiphyseal Cartilage. J. D. Bisgard, Omaha.—p. 412.
- The Psychologic Abdomen: Its Surgical Importance: Division I. B. L. Diamond, San Francisco.—p. 416.
- Post-Traumatic Pain Syndromes: Interpretation of Underlying Pathologic Physiology: Division II. W. K. Livingston, Portland, Ore.—p. 426.
- Differential Diagnosis of Jaundice: Division II. Symptomatology and Diagnosis of Hepatocellular Jaundice as an Aid in Its Distinction from Surgical Conditions. K. E. Hynes and C. R. Jensen, Seattle.—p. 435.
- Chemotherapy of Chronic Nonspecific Arthritis. H. E. Kimble, Chicago.—p. 440.

West Virginia Medical Journal, Charleston

34: 389-436 (Sept.) 1938

- Fat Embolism. P. H. Revercomb, Charleston.—p. 389.
- The Pediatrician and the Surgeon. J. T. Thornton, Wheeling.—p. 395.
- Analgesia in Labor. O. S. Reynolds, Franklin.—p. 399.
- Neurologic Problems and the General Practitioner. J. L. Wade, Parkersburg.—p. 407.
- The Nose and Its Owner. A. A. Seletz, Charleston.—p. 419.

Wisconsin Medical Journal, Madison

37: 781-872 (Sept.) 1938

- Scarlet Fever Immunization and Treatment. O. M. Layton, Fond du Lac.—p. 797.
- Scarlet Fever Immunization. A. B. Schwartz, Milwaukee.—p. 802.
- Scarlet Fever Immunization in a Group of Nurses. Ruth Caldwell Foster, Madison.—p. 804.
- Epithelioma of the Penis. G. H. Ewell, Madison.—p. 809.
- Use of Mandelic Acid in Urinary Tract Infections. A. Schlapik, Kenosha.—p. 814.
- Insulin and Metrazol Treatment in Schizophrenia. H. H. Reese, Madison, and A. Sauthoff, Mendota.—p. 816.
- *Prophylactic Use of Scarlet Fever Convalescent Serum: Analysis of Results in 1,061 Cases. M. Hardgrove, Milwaukee.—p. 821.

Prophylactic Scarlet Fever Serum.—Hardgrove states that of 1,179 questionnaires sent out to physicians using scarlet fever convalescent serum 1,061 gave information as to the age of the exposed individual, the number of days of exposure before receiving serum, the amount of serum used, the intimacy of contact, whether the patient was removed from the source of exposure, whether Dick tests had been performed and whether reactions occurred which could have been caused by the serum. Scarlet fever developed in the fourteen day period following the injection of convalescent scarlet fever serum in only twenty of the 1,061 cases. In twenty-two other cases a disease developed which may have been scarlet fever without rash (atypical scarlet fever). If this group of atypical scarlet fever cases, excluding two which occurred after fourteen days, is added to the group of fourteen-day true failures, it may be said that the serum failed to protect 3.77 per cent of the 1,061 individuals exposed. There were twelve cases in which early symptoms of scarlet fever were present at the time the serum was injected. In all these twelve cases the symptoms were relieved and no rash appeared. All of those in whom the disease developed within fourteen days were in the group of known intimate exposures. Reactions were observed in 1 per cent of the cases following the use of convalescent serum. These reactions consisted of slight transient elevations in temperature, occasional urticaria and joint pains lasting but a few days. When it is necessary for a susceptible contact to remain in the presence of a person with scarlet fever, convalescent serum should be given at intervals of ten days.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

Australian and New Zealand J. Surgery, Sydney

8: 1-112 (July) 1938

- Surgical Teaching in Germany. W. A. Osborne.—p. 5.
- The First Book on Surgery to Be Published in Victoria. K. F. Russell.—p. 17.
- Prostatic Obstruction. J. Smith Jr.—p. 19.
- *Treatment of Uremic Intoxication Complicating Pyloric Stenosis with Vomiting: Report on Two Cases Successfully Treated by Jejunostomy. M. A. Falconer and A. Lyall.—p. 37.
- Review of 100 Cases of Cancer of Stomach. F. G. Bell.—p. 57.
- Brief Review of Functional Hyperinsulinism: Report of Case Showing Improvement After Partial Pancreatectomy. J. M. Clarke.—p. 66.
- Gas Anesthesia: Critical Survey of Gas Anesthetic Technic. D. G. Renton.—p. 74.
- Etiology of Phlyctenular Ophthalmia. J. Barrett.—p. 80.

Uremic Intoxication and Pyloric Stenosis.—Falconer and Lyall believe that the usual routine treatment by frequent feedings of liquid food, cessation of alkalis and daily gastric lavage is not sufficient to correct uremic intoxication consequent to pyloric stenosis and that in many patients the administration of saline solution, either rectally or parenterally, is also required. Occasionally refractory cases of persistent vomiting are encountered and feeding by jejunostomy is indicated. Eight cases of pyloric stenosis with vomiting are presented, illustrating the effects of treatment by various preoperative methods. The first two patients died, one as the result of the persistence of vomiting and the other because a major operation was undertaken before the condition had been relieved. The third patient was treated by diet and gastric lavage and responded rapidly to the intravenous administration of hypertonic saline solution. Subsequently gastro-enterostomy was carried out and convalescence was short and uneventful. The fourth patient responded rapidly to simple methods of treatment of uremic intoxication following pyloric stenosis with vomiting. A few days later at laparotomy the diagnosis of cicatricial pyloric stenosis from duodenal ulceration was verified. Gastro-enterostomy was carried out and was followed by a short and uneventful convalescence. Death from pulmonary embolism occurred in the fifth case six days after gastro-enterostomy, which was performed after apparent improvement following saline solution subcutaneously and gastric lavage. At necropsy the kidneys showed macroscopic and microscopic evidence of a nephritis of mixed glomerular and interstitial types. This observation is of importance when correlated with the comparatively poor excretion of urea in the urine recorded throughout the period of observation. The sixth case is one of carcinomatous stenosis of the pylorus with vomiting. The marked improvement, after saline solution and acacia-dextrose solutions intravenously in the biochemical studies, was not accompanied by a corresponding degree of clinical improvement. Subsequent laparotomy disclosed a large carcinoma of the pyloric antrum of the stomach. Posterior gastrojejunostomy was carried out. Treatment by subcutaneous administrations of saline solution was unavailing; death occurred on the fifth day. The cause of death was not ascertained, as postmortem examination was not made. The remaining two patients who recovered show how uremic intoxication due to persistent vomiting from pyloric stenosis responds to feeding by jejunostomy. Routine methods were tried over a period of six days without apparent clinical benefit, but jejunal feedings were followed by a rapid and almost immediate improvement in both the clinical condition of the patient and the constituents of the blood. The levels of the plasma chloride were raised almost to the normal level by saline solutions intravenously, but little or no alteration was effected in the levels of the blood urea, which the authors believe give a better indication of the severity of the intoxication. Jejunal feeding should be maintained until the chemistry of the blood has returned to normal and the daily output of urine is adequate (from 1,000 to 1,500 cc.). When this stage is reached it is safe to undertake gastro-enterostomy, but as long as the tube remains in position there is no need for haste. For this second operation the abdomen may be opened by a left paramedian incision.

British Journal of Experimental Pathology, London

19: 239-272 (Aug.) 1938

- Growth of Proteus on Ammonium Lactate Plus Nicotinic Acid. P. Fildes.—p. 239.
 Disaggregation of Proteins by Enzymes. C. G. Pope.—p. 245.
 Crystalline Preparations of Tomato Bushy Stunt Virus. F. C. Bawden and N. W. Pirie.—p. 251.
 Some Protein Constituents of Normal Tobacco and Tomato Leaves: Note. F. C. Bawden and N. W. Pirie.—p. 264.
 Indophenol-Reducing Capacity of Guinea Pig Leukocytes. A. E. Kellie and S. S. Zilva.—p. 267.

British Journal of Radiology, London

11: 569-640 (Sept.) 1938

- X-Ray Studies of Closing of Ductus Arteriosus. A. E. Barclay, J. Barcroft, D. H. Barron and K. J. Franklin.—p. 570.
 The Physical and Biologic Basis of Grenz Ray Therapy. Z. A. Leitner.—p. 586.
 Some Direct Measurements of the Gamma Ray Dose Delivered to Malignant Lesions of the Tongue by Interstitial Irradiation. C. W. Wilson and S. Cade.—p. 599.
 Some Experiments in Tomography. G. B. Bush.—p. 611.
 Investigation into Dosage Delivered by Certain Techniques in Radiation Therapy of Carcinoma Cervix. B. Sandler.—p. 623.

British Medical Journal, London

2: 331-386 (Aug. 13) 1938

- Prevention and Control of Puerperal Sepsis, Including Its Medicolegal Aspects. R. W. Johnstone.—p. 331.
 Prevention of Puerperal Sepsis. Ethel Cassie.—p. 335.
 Prevention and Control of Puerperal Sepsis: Administrative Aspects. A. Massey.—p. 337.
 Id.: Bacteriologic Aspects. R. M. Fry.—p. 340.
 *Treatment of Undulant Fever with Neoprontosil. C. Z. Neumann.—p. 342.
 Comparative Test of Natural and Concentrated Antitoxin in Treatment of Malignant Diphtheria. B. A. Peters.—p. 344.
 Treatment of Pellagra with Nicotinic Acid. M. Rachmilewitz and Helen I. Glueck.—p. 346.

Treatment of Undulant Fever with Neoprontosil.—Neumann believes that, if the claims that he puts forward in the treatment of twenty cases of undulant fever are confirmed, neoprontosil and its congeners would be ideal remedies for the disease. Neoprontosil was administered intramuscularly to four patients, the dosage being one injection of 5 cc. on alternate days. The results were disappointing in three cases. During the first week of the fourth patient's (a boy 6 years of age) illness the temperature was as high as 104 F. and the reaction of the blood serum was strongly positive to *Brucella melitensis*, at which time he was treated with intramuscular injections of neoprontosil on alternate days; at the third injection the temperature was 100 F. in the evening and he was completely afebrile on the tenth day of treatment. No second wave of pyrexia occurred, although the patient was kept under observation for six months. In the light of further experience with neoprontosil by mouth it is probable that the dosage administered intramuscularly was too small. Sixteen patients were treated with neoprontosil orally; they were mostly children and the results were gratifying. The initial dosage for children was four tablets of neoprontosil daily. Youths and adults received six tablets. After three or four days, according to the gravity of the case and its response to treatment, the number of tablets was reduced to three in the case of children and to four or five tablets in adults. Usually at the end of a week children were given two tablets and adults three tablets daily, and this was continued for a few days. It is advisable to give the drug for several days after the patient has become afebrile. The effect of the drug on the temperature is usually prompt, and a daily fall of 1 degree F. may be expected. In fifteen of the sixteen cases the average duration of the fever was seven days, ranging from two to twelve days, and in one the drug was apparently ineffective. If no result is evident within a week, the drug will be ineffective even after prolonged administration. If it is given early in the course of the disease, the patient can often return to school or to work within two or three weeks after treatment has been started. No severe toxic effects were observed after the oral administration of neoprontosil. In three cases slight vomiting occurred during the treatment and in one case strangury; both these symptoms disappeared in a day or two when the dose was diminished. In two cases a slight degree of cyanosis of the cheeks was seen. In the two cases in which treatment was not continued for a few days after they became

afebrile the pyrexia reappeared, but it vanished promptly when neoprontosil was again given. Most of the patients were treated in the acute stage of the disease, and more experience in the chronic cases of undulant fever would be desirable.

Clinical Science, London

3: 247-356 (Aug. 15) 1938

- Unilateral Loss of Blood Pressure Raising, Pulse Accelerating, Reflex from Voluntary Muscle Due to Lesion of Spinal Cord. M. Alam and F. H. Smirk.—p. 247.
 Observations in Man Concerning Effects of Different Types of Sensory Stimulation on Blood Pressure. M. Alam and F. H. Smirk.—p. 253.
 Blood Pressure Raising Reflexes in Health, Essential Hypertension and Renal Hypertension. M. Alam and F. H. Smirk.—p. 259.
 Results of Sympathetic Stimulation and Extirpation on Human Electrocardiogram. E. N. Chamberlain.—p. 267.
 Further Observations on Vascular Responses of Human Limb to Body Warming; Evidence for Sympathetic Vasodilator Nerves in Normal Subject. R. T. Grant and H. E. Holling.—p. 273.
 Pathologic Changes in Arteries Supplying Fingers in Warm Handed People and in Cases of So-Called Raynaud's Disease. T. Lewis.—p. 287.
 *Raynaud's Disease and Preganglionic Sympathectomy. T. Lewis.—p. 321.
 Mechanism of Local Sweating in Response to Faradism. R. G. Bickford.—p. 337.
 Acute Arterial Lesions in Rabbits with Experimental Renal Hypertension. C. Wilson and G. W. Pickering.—p. 343.

Raynaud's Disease and Preganglionic Sympathectomy.—Lewis examined six unselected patients with "Raynaud's disease" shortly after preganglionic sympathectomy. Discoloration of the fingers occurred spontaneously or was induced within a few days of operation in three. In one of these three cases the fingers presented nutritional changes; in another there was no trace of such changes. In only two of the remaining three cases could attacks be induced before operation (and in one of these with difficulty); in these two abnormality in the reaction of the fingers to cold could be shown after operation. Preganglionic sympathectomy does not bring the fingers of these patients to a common state; it does give relief, but a local abnormality remains, and this can be displayed in a measure that is related to the abnormality displayed before operation. The attacks in "Raynaud's disease" are not due primarily, as Raynaud thought, to excessive action of the vasomotor nervous apparatus. They are due primarily to a local fault; this may consist of occlusive structural disease or it may not. In the latter instance the digital vessels appear to present increased susceptibility to cold, the reason for which still remains obscure. The full vasodilatation resulting from preganglionic sympathectomy declines during a period of about a week following operation.

Glasgow Medical Journal

12: 53-108 (Aug.) 1938

- History of Circulation. L. Aschoff.—p. 53.
 Trend of Radium Therapy. A. A. Charteris.—p. 76.

Indian Medical Gazette, Calcutta

73: 449-512 (Aug.) 1938

- Leptospirosis in India. B. M. Das Gupta.—p. 449.
 Peptic Ulcer in Northern Circars: Note on Incidence. M. Narasimha Rao.—p. 454.
 Vitamin B and Peptic Ulcer. M. Narasimha Rao.—p. 457.
 *Treatment of Phrynoderma by Vitamin A Concentrate. M. V. Radhakrishna Rao.—p. 461.
 Studies on Potency of Prophylactic Vaccines: I. Cholera Vaccine. C. L. Pasricha, D. N. Chatterjee and B. M. Paul.—p. 463.
 Spontaneous Subarachnoid Hemorrhage. R. N. Chaudhuri.—p. 466.
 Illustrations Explaining an Article on Siphunculina Funicola (Eye-Flu). M. M. Syddiq.—p. 468.
 Effect on Rats of Supplementing a North Indian Diet with Vegetable Proteins (Sprouting Pulses) and Calcium. R. K. Pal and N. Singh.—p. 469.
 Volvulus as Cause of Intestinal Obstruction. M. G. Kini and D. Venkoba Rao.—p. 471.
 Spinal Anesthesia. C. H. Bliss.—p. 474.
 Incidence of Pulmonary Tuberculosis in the Punjab Villages. B. L. Kanra.—p. 477.

Vitamin A Concentrate in Phrynoderma.—Radhakrishna Rao presents two representative cases of papulofollicular dermatosis (phrynoderma) commonly seen in malnourished individuals. While it is generally agreed that phrynoderma is a separate clinical entity associated with malnutritional states, the exact cause of the condition is still not quite clear. Treatment consisted in giving from 10,000 to 18,000 international

units of a vitamin A concentrate daily. Each cubic centimeter of this concentrate, which contains no added vitamin D, contains 72,000 international units of vitamin A. No alteration was made in the diet and no local medication was applied. The results of treatment over a period ranging from fifty to 140 days were satisfactory, but they were not definitely conclusive, as the controls also showed slight improvement during the period of observation.

Journal of Laryngology and Otology, London

53: 485-556 (Aug.) 1938

Some Factors in Relationship of Upper Respiratory Infection and Bronchiectasis. G. E. Hodge.—p. 485.
Presence of Blood in Air Passages After Tonsillectomy. T. Leegaard.—p. 499.

Journal Obst. & Gynaec. of Brit. Empire, Manchester

45: 597-768 (Aug.) 1938

Trichomoniasis. J. R. Goodall, F. O. Anderson and F. L. MacPhail.—p. 597.
Etiology of Pregnancy Toxemia. R. W. Nichol.—p. 609.
Causes of Fetal Death in Ceylon: Study of 1,000 Consecutive Cases of Stillbirth. G. A. W. Wickramasuriya.—p. 622.
*Prophylaxis of Constriction Ring Dystocia. M. H. Phillips.—p. 638.
Tubal Pregnancy. B. Solomons.—p. 644.
Transposition (Interposition) of the Uterus for Severe Uterine and Vaginal Prolapse. J. St. G. Wilson.—p. 655.
Unusual Congenital Abnormality of the Vagina. A. A. Gemmell, H. F. Woolfenden and J. E. Frazer.—p. 663.
Subcutaneous Hemangio-Endotheliomas Associated with Pregnancy. A. Davis.—p. 667.
Pregnancy in Bicornute Uterus. O. Browne.—p. 674.
Parallel Duplication of Face in an Anencephalic Fetus. G. Maizels.—p. 679.
Severe Ulceration of Vulva and Vagina During Pregnancy, Treated by Administration of Vitamins: Case. E. A. Gerrard.—p. 683.
Infibulation and Female Circumcision: Study of Little Known Custom. A. Worsley.—p. 686.
Intra-Uterine Amputations and Annular Constrictions in a Living Infant, Now a Child of 4, Due to Amniotic Adhesions Resulting from Oligohydramnios. Y. N. Ajinkya.—p. 692.

Prophylaxis of Constriction Ring Dystocia.—Phillips believes that the localized contraction of the uterus, constriction ring, is always preceded by a longer or shorter period of that painful and ineffective activity of the uterus, well described by the old clinical term colicky action of the uterus. Colicky action of the uterus can be recognized by the simple clinical observation that the painfulness of the uterine contraction persists after the palpable hardening brought about by uterine contraction has passed off. Prompt recognition and unremitting treatment of this colicky action until it has ceased will prevent the onset of a constriction ring and so do away with one of the most vexatious and dangerous complications of labor. The author's practice now is, when these troublesome colicky pains are suspected, immediately to place his hand on the uterus and to get the patient to describe the exact duration of the pain she is experiencing. Should it extend to or beyond the cessation of the uterine contraction, one can be certain that colicky action has started. It must be controlled at once by an efficient antispasmodic drug. Preparations of opium are probably the best. The patient must be watched as the influence of the drug ceases. With his hand again on the uterus, the duration of the pain is estimated. The drug must be repeated in this way until the colicky action of the uterus has ceased. The pain is always referred to the lower part of the abdomen, just above the pelvic brim, often on one side only. It may begin at or soon after the onset of labor or not until after several or even many hours of feeble infrequent contractions. It may be severe or even excruciating. These are variable features, but invariably the pain will be found to persist after a contraction has passed off. The colicky action always begins in and is usually confined to the first stage of labor, whereas the constriction itself, which may follow, usually occurs in or is at least first recognized in the second stage. With each severe pain the woman often struggles and strains. Observing her behavior, the attendant is led to think that she is really in the second stage of labor and she may be urged and encouraged to bear down—a useless effort which may well aggravate the spasm. Puzzled at the delay in delivery, in spite of all these pains and efforts, the attendant is liable to make frequent vaginal examinations, again a procedure which will intensify the spasm. Even abdominal

palpation is liable to irritate such a uterus. But worst of all is the modern blunder—in ignorance of the real state of things—of giving the injection of pituitary extract, which is so effective in properly selected cases of real second-stage delay due to feeble uterine action.

Journal of Pathology and Bacteriology, Edinburgh

47: 1-204 (July) 1938

Darkground Studies of Flagellar and Somatic Agglutination of Bacillus Typhosus. A. Piiper.—p. 1.
The Clitoris of the Rat After Ovariectomy and Injection of Sex Hormones. Kathleen Hall.—p. 19.
Abnormal Flocculation Reactions with Diphtheria Toxoid. Mollie Barr and A. T. Glenny.—p. 27.
Metastatic Deposit of Bronchial Carcinoma in a Hydrocele Misdiagnosed "Endothelioma," with a Review of Supposed "Endotheliomas" of Serous Membranes. R. A. Willis.—p. 35.
Endothelioma of the Pericardium. J. C. Dick.—p. 43.
Transmission of the Rous Filtrable Agent to Normal Tissues of Fowls. E. Mellanby.—p. 47.
Fibroma Virus Infection in Tamed Rabbits. C. G. Ahlström and C. H. Andrewes.—p. 65.
Transplantable Sarcoma Occurring in Rabbit Inoculated with Tar and Infectious Fibroma Virus. C. H. Andrewes and C. G. Ahlström.—p. 87.
Hemangioblastoma of Sacrum. R. J. V. Pulvertaft.—p. 101.
Histologic Investigation of Development and Structure of the Human Lung. Eugenia R. A. Cooper.—p. 105.
Histologic Study of the Mummy of Har-Mosé, Singer of Eighteenth Dynasty (circa 1490 B. C.). A. F. B. Shaw.—p. 115.
Unusual Variant of Friedländer's Bacillus and Its Relation to Rugose Variant of Vibrios. L. E. Shinn.—p. 125.
Influence of Injection of Foreign Proteins on Normal Bactericidal Activity of Serum. S. Thomson.—p. 131.
Cytoplasmic Inclusion Bodies in Engorging Tick. J. D. Gregson.—p. 143.

Lancet, London

2: 351-408 (Aug. 13) 1938

Cancer Research: The Past and the Future. E. C. Dodds.—p. 351.
*Sulfanilamide in Gonorrhea: Analysis of 633 Cases. A. J. Cokkinis and G. L. M. McElligott.—p. 355.
Some Anomalous Hyperchromic Anemias. M. C. G. Israëls and J. F. Wilkinson.—p. 362.
Operative Cholangiography: Its Contribution to Physiopathology of the Common Bile Duct. P. L. Mirizzi.—p. 366.
Adenoid Epithelial Tumor of Submaxillary Gland, with Discussion on Nature of So-Called Mixed Tumor of Salivary Gland. M. G. Kini and P. R. Rao.—p. 369.
Lumbar Puncture in Outpatients. D. Erskine and A. G. Johnson.—p. 371.

Sulfanilamide in Gonorrhea.—Cokkinis and McElligott discuss the final results of 491 consecutive male and 142 female cases of gonorrhea. They find that the best results with sulfanilamide treatment in gonorrhea can be obtained only by a specialized technic of administration and that incorrect or haphazard chemotherapy is followed by a high proportion of failures. With this optimal technic a permanent cure can be expected in 80 per cent of male patients with one course of treatments extending over three weeks, although all manifestations of the disease usually clear up well within the first week. With additional courses in cases that are resistant or in relapse, the total permanent cures in male patients can be increased to more than 90 per cent. Under optimal conditions the disease in women appears to react equally well to the drug, but these conditions are more difficult to attain because women are more sensitive to its minor toxic effects. A degree of immunity appears to be essential to the attainment of optimal results with sulfanilamide chemotherapy. Hence the importance of "timing" the chemotherapy correctly and combining it with vaccine treatment. 1. To males with acute infections attending in the first week of symptoms, vaccine treatment is started at once and continued twice a week (starting with 5 and increasing to 100 million) through the chemotherapy. Daily irrigations are given. Sulfanilamide is started from eight to ten days after a discharge has commenced and continued for a full three weeks. The daily dose varies with weight, the usual dose being 4 Gm. daily (0.5 Gm. in a glass of water after the four daily meals). This is continued for the first two weeks, after which it may be diminished to 3 Gm. daily. An alkaline mixture may be given if desired and the patient is seen at least twice a week. A list of instructions is issued, pointing out the importance of strict obedience and absolute continuity of treatment and containing usual directions about avoiding eggs, onions and saline purges as well as prolonged exposure to sunlight. After three weeks

all treatment is suspended and the patient attends weekly for prostatic bead tests, urethroscopy being done on one of these visits. If these are satisfactory, provocative tests are started from three to four weeks later. After passing all tests the patient is kept under observation for a further six to eight weeks, when at least one more provocative test is given before final discharge. If the first course fails or relapse occurs an interval of at least two weeks must elapse before the next course is started. During this interval and after it a mixed gonococcus vaccine is given, while prostatic massage and diathermy are added in cases in which the prostate is enlarged. Patients who fail to react after ten days should be given up as failures for that course, and a further course administered in three weeks. 2. After the first week of symptoms in acute cases the technic is the same, except that sulfanilamide is started at once. Complicated infections can be expected to respond as rapidly as uncomplicated ones. 3. The dosage in patients with chronic infections need not exceed 3 Gm. daily and the total period may be cut down to about seventeen days, while a mixed gonococcus vaccine may be used with advantage. 1. In recent infections in women, vaccine treatment is started at once and continued biweekly as in men. Daily treatment consists only of urethral and vaginal irrigations. In the presence of dysuria an alkaline sedative is given. Sulfanilamide is never commenced before the eighth day of symptoms and is administered continuously for three weeks. An adequate daily dose is 3 Gm. At the end of three weeks, if all tests and examinations are negative, treatment is suspended. The patient is examined fortnightly for one month and then after each menstrual period for a further two months, when a provocative injection of vaccine (500 million gonococci) is given. If tests made two days after this are negative and clinical signs are absent, the patient may be regarded as cured. 2. In women patients who failed to react to the foregoing treatment or in whom the infection relapsed, three weeks should elapse before a further course of sulfanilamide is given. This further course is recommended particularly in cases of proved gonococcal relapse. In the more common relapses due to secondary organisms, the associated vaginitis is treated for two weeks with acetarsone pessaries and daily douches, while a further course of sulfanilamide may be given if no improvement occurs. 3. In women with a chronic infection similar chemotherapy is employed, but acetarsone pessaries are used from the beginning and a mixed gonococcus vaccine is given.

Medical Journal of Australia, Sydney

2: 185-224 (Aug. 6) 1938

- Chemistry and Medicine. A. S. Walker.—p. 185.
Some Common Eye Injuries and Disorders. B. Moore.—p. 191.
Blood Supply of Visual Pathways. A. A. Abbie.—p. 199.
*Probable Vector of Endemic Typhus in New Guinea. C. E. M. Gunther.—p. 202.

2: 225-264 (Aug. 13) 1938

- Vitamins in Nutrition of Children. D. Vickery.—p. 225.
Nutrition of Children. E. H. M. Stephen.—p. 228.
Nutrition of the Child. F. S. Hansman.—p. 233.
Psychology, Baby Health and Child Welfare. C. Swanton.—p. 235.
The Problem of the Partially Sighted. J. Barrett.—p. 242.
Some Recent Advances in Physical Therapy. E. P. Dark.—p. 243.

Probable Vector of Endemic Typhus in New Guinea.

—During the last four years Gunther has collected and examined approximately 3,000 larval mites, comprising fourteen species from seventeen hosts. All the species, except certain specimens of *Schöngastia yeomansi*, were collected in the Morobe district of New Guinea. Of all the mites collected, approximately 90 per cent were *Trombicula hirsti*, variety *morobensis*, and of this species nearly all were taken from various common birds. A small number were taken from seven bandicoots and from three men. The only other species taken from man was *Schöngastia yeomansi*, in another district. Since no cases of endemic typhus have been reported from the Aitape district, consideration of *Schöngastia yeomansi* as a possible vector must be shelved. *Trombicula hirsti*, variety *morobensis*, is the most likely suspect. In the Morobe district it constitutes about 90 per cent of all mites taken and is the only species which has so far been found on man. Its presence in such overwhelming numbers is certainly due to its affinity for various common birds. The presence of this species in such large numbers is not incon-

sistent with the possibility of its being the vector, as the majority of those attacking man must come from birds; but a minority must come from bandicoots. Three of the less common species, *Neoschöngastia clauda*, *Neoschöngastia callipygea* and *Waldia buloloensis*, occur on the various rodent hosts, and any one might be the direct vector to man. There is no reason to suppose that they would not attack man; *Schöngastia yeomansi* has been found to do so, proving that this habit is not confined to the genus *Trombicula*. In such a case, however, it is certain that the bandicoot would be infected by either of the first two species, and *Trombicula hirsti*, variety *morobensis*, could also act as a vector. The author regards this last as the probable vector, from bandicoot to man, and the others as the probable vectors between the various rodents. *Neoschöngastia riosi* and *Schöngastia rotunda* are apparently only occasional parasites of the bandicoot and appear to be unlikely vectors. The seven remaining species, because they are confined to birds, are quite unlikely to be vectors.

Practitioner, London

141: 237-356 (Sept.) 1938

- Sex Education and the General Practitioner. H. Ellis.—p. 237.
Sexual Development of the Child and Adolescent. H. Crichton-Miller.—p. 243.
Sex Problems in Marriage. J. A. Hadfield.—p. 252.
Problems of Celibacy in the Male. K. Walker.—p. 263.
Sex Problems of the Single Woman. Laura Hulton.—p. 270.
Homosexuality. D. Curran.—p. 280.
Local Anesthesia and Analgesia. W. H. C. Romanis.—p. 288.
Splints for the Practitioner. W. Mercer.—p. 300.
Speech Defects in Childhood. W. G. Wyllie.—p. 310.
Treatment of Asthma in Childhood. C. P. Lapage.—p. 318.
Purchasing a Practice Through Insurance. G. Lowe.—p. 328.

Quarterly Journal of Medicine, Oxford

7: 331-494 (July) 1938

- Output of the Heart in Congestive Failure. J. McMichael.—p. 331.
Clinical Value of Estimation of Levulose Tolerance by Means of Analysis of Blood Levulose. Freda K. Herbert and G. Davidson.—p. 335.
*Pulmonary Tuberculosis Complicating Diabetes Mellitus. H. P. Hinchworth.—p. 373.
Role of Copper in Iron Deficiency Anemia in Infancy. J. H. Hutchison.—p. 397.
Dyspnea: Review. K. V. Christie.—p. 421.
Cardiac Aneurysm. J. Parkinson, D. E. Bedford and W. A. R. Thomson.—p. 455.
Genetics of Transposition of Viscera. E. A. Cockayne.—p. 479.

Tuberculosis and Diabetes Mellitus.—Himsworth states that pulmonary tuberculosis was found in fifteen (6.5 per cent) of 230 consecutive cases of diabetes mellitus on their first attendance at the hospital. Two of these patients had tuberculous bronchopneumonia and were readily diagnosed by clinical methods. In the remaining thirteen the diagnosis was made only by x-ray examination. The conclusion is drawn that early pulmonary tuberculosis in the diabetic patient is impossible to diagnose by clinical methods and that a routine roentgenogram of the chest is essential in every diabetic person when he is first seen. The x-ray examination should be repeated every year, or more often if the control of the diabetes is unsatisfactory. The x-ray appearances of the early pulmonary tuberculosis in diabetes are those of a chronic inflammatory lesion, they are identical in appearance with new lesions appearing in the lungs of proved cases of pulmonary tuberculosis and they can progress until they are roentgenologically, and the cases clinically, typical of pulmonary tuberculosis; they are quantitatively correlated with clinical evidence of toxemia. Evidence is brought forward that uncontrolled diabetes predisposes to the development of the pulmonary lesion and conversely that treated diabetic patients are no more liable to develop pulmonary tuberculosis than nondiabetic subjects. When the two diseases are associated, the treatment of the diabetes is of primary importance. The prognosis is excellent if the pulmonary lesion is discovered at an early stage.

Tubercle, London

19: 481-528 (Aug.) 1938

- Investigations on Tuberculosis Among Students in Scandinavia. J. L. Jacobs.—p. 481.
Increase of Typhoid Agglutinins in Tuberculosis (Amnesic Reaction). P. D. Crimm and D. M. Short.—p. 491.
Contacts with Sputum Positive Tuberculous Cases. Enid Williams.—p. 495.

Journal Belge d'Urologie, Brussels

11: 353-418 (Aug.) 1938

- Contribution to Physiologic Study of Ureter. P. Mingers.—p. 353.
- First Impressions on New Mode of Administration of 1162 F.: Intravenous and Intramuscular Injections of Strong Concentrations of Sulfanilamide (25 Per Cent). J. Decoux.—p. 373.
- *Action of Derivatives of Sulfanilamide on Spermatogenesis. M. Vigoni.—p. 375.

Sulfanilamide Derivatives and Spermatogenesis.—Vigoni points out that several months ago Jaubert and Motz reported in the French biologic society that certain sulfanilamide products exert an inhibiting effect on the spermatogenesis. Since this report was circulated widely, the author reviews the observations of Jaubert and Motz and then reports his own investigations on this problem. He studied the spermatogenesis in healthy subjects, in gonorrheal patients treated with the old therapeutic measures, and in gonorrheal patients treated with para-aminophenylsulfamide. The total number was forty-three. In healthy subjects it was observed that the number of spermatozoa varies greatly but that their motility is always good. In gonorrheal patients who were treated with the old methods there were likewise considerable variations in the number of spermatozoa, but on the whole the numbers were inferior to those in healthy subjects; however, it was impossible to establish a relationship between the diminution and the degree of acuteness of the gonorrhea. The motility of the spermatozoa was normal in the chronic cases or in those in which cure was effected but was subnormal in the acute cases. Regarding the spermatogenesis of gonorrheal patients who had received para-aminophenylsulfamide, the author says that, as in the other groups, the number of spermatozoa varied greatly in the different patients. In two cases azoospermia existed. There was no relationship between the quantities of para-aminophenylsulfamide absorbed by the patients and the number of spermatozoa. Some subjects, who had received only a small amount of the medication, had an extremely small number of spermatozoa, while others, who had received rather large doses, had normal or supernormal numbers of spermatozoa. The motility of the spermatozoa, on the other hand, seems to be more often impaired in these patients who were subjected to chemotherapy than in those treated with the old methods. However, this impairment of the motility ceases later on; after an interval of a month had elapsed it had disappeared in all but one of the patients. Of the two patients with azoospermia, only one could be examined later and in this one numerous motile spermatozoa were detected.

Journal d'Urologie Médicale et Chirurgicale, Paris

46: 1-96 (July) 1938

- Technic of Transurethral Resection of Prostate. J. Cibert.—p. 5.
- *Renal Disorders and Surgery of Kidney in Cases of Deformities of Vertebral Column. G. Jasienski.—p. 15.
- Neosphenamine in Treatment of Gonorrheal Orchiepididymitis. J. Conradt.—p. 29.
- *Glandular Therapy of Hypertrophy of Prostate. A. Cassuto.—p. 34.

Renal Disorders and Deformities of Vertebral Column.—Jasienski calls attention to the fact that renal disorders occasionally are related to deformities of the vertebral column. Congenital scolioses are often associated with congenital malformations of the urinary passages; or the same morbid factor, such as tuberculosis, may cause a deformity of the vertebral column and renal or other urinary disorders. In other cases, one of these disorders causes the other one. The deformity of the vertebral column may be secondary to the primary disorder of the kidney and vice versa. Among the different spinal deformities it is scoliosis which most frequently concurs with renal disorders. An extraordinarily high incidence of chronic appendicitis has been demonstrated in scoliotic children. On the other hand, scoliosis has been observed in the course of renal disorders such as lithiasis, nephritis, paranephric abscess and floating kidney. The author discusses the theories that have been advanced with regard to the pathogenesis of the so-called nephrogenic scolioses and cites his own observations on this problem. He encountered scoliosis quite frequently in renal disorders. In acute renal disturbances it is more the rigidity of the vertebral column than the scoliosis which draws

the attention. In a patient who received surgical treatment for a subphrenic abscess, the author was able to observe the development of a spinal concavity toward the diseased side. He further shows that a deformity of the vertebral column can exert an unfavorable influence on the superior urinary passages. Such a deformity creates unfavorable mechanical conditions for the renal function and the discharge of the urine and thus provokes disorders in the urinary passages. Hydronephrosis, floating kidney, lithiasis and other disorders occur in such patients. Necroses on persons with deformities of the axis of the vertebral column frequently reveal irregularities in the position and shape of the kidney, of the pelvis and of the ureters. The author further states that kyphosis resulting from a tuberculous spondylitis may cause disorders in the urinary tract and he cites authors who observed that Pott's disease is often accompanied by renal lithiasis or by renal tuberculosis. After pointing out that Frangenheim was of the opinion that the lumbar incision should not be employed in patients with considerable scoliosis, he evaluates the different methods that permit nephrectomy in patients with Pott's disease and other deformities of the vertebral column. In the conclusion he points out that, if the impossibility of a lumbar incision becomes evident, two angular anterior incisions should be made: an abdominal one and one along the eleventh rib, which, after liberation of the rib, permits the opening of the tenth intercostal space. He thinks that the incision suggested by Uteau as well as the thoracophrenolaparotomy should be resorted to only in exceptional cases.

Glandular Therapy of Prostatic Hypertrophy.—Following a discussion of the development of the surgical treatment of hypertrophy of the prostate, Cassuto points out that, in view of the fact that the onset of the hypertrophy frequently coincides with a diminished genital function, it has been assumed that the arrested or diminished testicular function is intimately connected with the causation of the hypertrophy. He surveys the literature on the glandular therapy of hypertrophy of the prostate and describes his own experiences with this treatment in thirty-five cases. The results varied. In some the symptoms diminished to the point at which treatment could be discontinued, in others the improvement was only temporary, and in still others there was no effect even after prolonged treatment. In analyzing the effects of glandular therapy on the principal symptoms of hypertrophy of the prostate, the author found that pollakiuria was influenced most effectively; it was favorably influenced in at least twenty-six cases. The anatomic status of the prostate remained nearly always the same, except that in five cases the firmness seemed to be lessened and it even had the appearance of there being a reduction in the hypertrophy. The improvements were obtained in a minimum period of one or two months. If the effect is negative after such a period, the treatment must be changed. The azotemia seems to be improved only in those cases in which there is an appreciable clinical amelioration. In the author's material this occurred in ten of the cases. He employed glandular therapy in addition to surgical treatment in six cases. The postoperative course in these cases was not sufficiently different from the usual course to draw definite conclusions. Testosterone propionate was used.

Presse Médicale, Paris

46: 1233-1248 (Aug. 13) 1938

- *Functional Test of Venous Circulation. D. Olmer, A.-X. Jouve and J. Vague.—p. 1233.
- Renal Insufficiency by Habitual Absolute or Relative Oliguria. J. Cottet.—p. 1235.

Functional Test of Venous Circulation.—Olmer and his associates say that the venous circulation is the expression of the combined play of several factors, the most essential of which are insufficiency of the right ventricle, the condition of the large venous trunks and the peripheral venopressure mechanism. The venous pressure, when considered alone, does not permit the definite determination of the functional capacity of the right side of the heart. The authors describe a functional test which they employed systematically for one year in patients likely to present modifications of the venous circulation. In order to explore at the same time the peripheral and the hepatportal sections of the venous system, they combine the passive raising

of the lower extremities with hepatic compression. The technic is as follows: The patient is in a strictly horizontal position. Then the lower extremities are elevated 60 degrees above the level of the bed; it is essential that the patient remain passive in order to eliminate the play of the muscular contractions; the elevated position is maintained for fifteen seconds. After the inferior members are lowered again, the patient remains in the horizontal position for fifteen seconds. Then hepatic compression is done by pressing the right hand against the anterior surface and the left hand against the flank. The pressure should be moderate so as not to become painful. It is maintained for fifteen seconds. The brachial venous pressure is determined five times: during rest, during the elevation of the inferior members, during the subsequent rest period, during the hepatic compression and after another fifteen seconds of rest. The test requires one minute. The venous pressure is measured by means of the phlebopiezometer of Villaret or by the manometer of Claude. The authors report their experiences with this test on thirty normal subjects and on patients with various pathologic conditions. They found that this functional test of the venous circulation is always positive in cases of insufficiency of the right side of the heart or in total asystole. The evaluation of the results obtained with this test indicates that it permits the determination of the functional capacity of the heart as regards the venous circulation.

Schweizerische medizinische Wochenschrift, Basal

GS: 1005-1024 (Aug. 27) 1938

Delivery in Case of Narrow Pelvis. H. Wespi.—p. 1005.

Organization of Scientific Bacteriology. O. Veraguth.—p. 1012.

*Schüller-Christian's Disease. M. Esser.—p. 1014.

Aspects of Hypersensitivity to Medicaments. N. Markoff.—p. 1016.

Five Years' Experiences with Spirochetal Vaccine Hilgermann. L. Spitzer.—p. 1017.

Schüller-Christian's Disease.—Esser, after citing the triad of symptoms of the Schüller-Christian syndrome, namely cranial defects, diabetes insipidus and exophthalmos, says that Rowland considered xanthomatous proliferations as the cause and that Ludwig Pick classified the disease with the essential lipoidoses. However, investigations and observations during recent years made it appear doubtful that a disturbance in the lipid metabolism is the cause of the disease, because anatomic studies disclosed that proliferation of reticulo-endothelial elements and granuloma formation precede the depositing of lipoids. The author reports his observations on a child with Schüller-Christian's disease who was under his observation for three years and who is now practically cured. The child came under his observation in April 1935, at the age of 14 months. During the winter the child had had fever and coryza repeatedly, and in the last few weeks the parents had noticed a swelling in the temporal regions. In the course of the examination roentgenoscopy disclosed the cranial changes that are typical for Schüller-Christian's disease. After describing the results of the chemical and morphologic examinations of the blood, the author says that he regards as especially significant the reticulated giant cells, some of which contained cocci, and the foam cells and the debris of foam cells. The sternal punctate disclosed a reduction in the myeloid elements and an increase in the small reticulated cells. Moreover, the author detected in the bone marrow a reticulated giant cell which was filled with cocci to such an extent that it gave the impression of a bacteriologic culture. Under the influence of the customary treatment with a diet that was deficient in fat and free from cholesterol, the general condition became so much worse that the proposed therapeutic diet had to be interrupted and a mixed diet instituted. The cranial defects increased and at the end of three months the child was discharged from the hospital without showing improvement. In the course of the examination Letterer, Sherman, van Crefeld case the author recalled that Letterer, Sherman, van Crefeld and others had observed an infectious reticulo-endotheliosis in which bone defects and cocci were found. On the basis of a discussion of the possible development of this disorder, the author decided to try a diet which was rich in lipoids and fat. In addition to a mixed diet the child was given daily from two to four egg yolks and large amounts of milk. From now on

the cranial changes became fewer and gradually disappeared again. Today the child is well; the cranial defects and changes in the blood have disappeared; only the number of thrombocytes is still increased. At present the author is ing another child with Schüller-Christian's disease. Here the skeletal changes are accompanied by hematic disorder; the reticulated giant cells again have masses of cocci. On basis of these observations the author concludes that Schüller-Christian's disease is of infectious origin.

Dermosiflografo, Turin

13: 401-466 (July) 1938. Partial Index

Vitamin B₁ in Alopecia Areata (Celsi). F. Lisi.—p. 401.

*Familial Spinulous Keratosis: Cases. G. Perpignano.—p. 442.

Cutaneous Blastomycosis from *Wuilemin* and *Albicans* Endomyces with Grave Septicemia: Case. T. Venturi.—p. 450.

Familial Spinulous Keratosis.—Perpignano reports three cases of chronic spinulous keratosis of the neck, thorax and extremities in a man aged 29 and his two children aged 5 and 3 years. None of the patients suffered from endocrine disease or had a history of poisoning from intake of drugs. All were frail, with enlarged laterocervical, axillary and inguinal lymph nodes, and showed signs of chronic bronchitis on auscultation. In all cases the Wassermann and Meinicke turbidity tests for syphilis were negative, the sputum was negative for tubercle bacilli and the skin reaction to tuberculin gave positive results. There was a history of pulmonary tuberculosis in the mother. The roentgen examination of the thorax showed slight changes of the lung of the father and the presence of tracheal bronchial adenopathies in one of the children. The author believes that in these cases there was hereditary predisposition to the development of cutaneous diseases which was due to stimulation of the skin by tuberculous toxins. He calls attention to the possible pathogenic role of latent tuberculosis in skin diseases.

Archivos Argentinos de Pediatria, Buenos Aires

9: 585-724 (June) 1938. Partial Index

*Immunotransfusion in Children. M. Acuña and I. Fernández.—p. 585.

Urobilin and Blood in Anemia of Premature Newborn Infants: After Treatment. Perlina Winocour.—p. 596.

Hemiplegia After Tonsillectomy: Case. A. Gareiso and F. Escobar.—p. 610.

Favorable Evolution of Lipoid Nephrosis in Intercurrent Measles. C. Montagna and A. A. Rimoldi.—p. 617.

Immunotransfusion in Children.—Acuña and Fernández resorted to immunotransfusion in sixteen cases of grave infections, especially pneumonia and bronchopneumonia, in infants and children. In all cases the treatments previously given failed. The intervals between transfusions varied from one to two days, the total number of transfusions varied from two to ten, and in rare cases ten, and the total amount of blood for transfusion varied from 20 to 170 cc. Only in rare cases as much as 260 cc. of blood given at one time. The authors stress the advisability of selecting strong, healthy donors without history of syphilis or malaria. Polybacterial vaccines prepared with bacteria killed by heat, or stock vaccine autovaccines prepared from the patient's secretions, were used in immunizing the donors. Several donors were prepared consecutively to avoid the constant use of one person. Blood was taken from four to six hours after injection of vaccine. Transfusion was preceded by removal of some of the patient's blood and given slowly by gravity to prevent overcharging of the heart. It was given through the veins, preferably through the longitudinal sinus, in amounts of from 20 cc. of a 0.5 per cent citrated blood for each kilogram of body weight. There were no accidents. One patient of the group of sixteen died. The authors conclude that immunotransfusion is of therapeutic value in infections, especially pneumonia and bronchopneumonia, in infants and children. Earlier administration of the treatment, the better the results. Transfusion must be repeated for good results. If done the proper technic and under the necessary precautions, it is tolerated by infants and children. The selection of bacterial strains and the type of vaccines used in immunizing the child are determined by the individual case.

Pediatrica Pratica, São Paulo

9: 185-293 (May-June) 1938

- *Technic for Pneumococcic Pleural Empyema in Infants. A. Gomes de Mattos.—p. 185.
Ascorbic Acid in Treatment of Certain Stomatitides. J. F. Barretto.—p. 235.
Complications and Sequels of Grip. M. Schaehtler.—p. 240.

Pneumococcic Pleural Empyema.—In the treatment of pneumococcic pleural empyema in infants, Gomes de Mattos reports satisfactory results from intrapleural injections of air, followed by lavage of the pleural cavity with a 0.5 per cent solution of ethylhydrocupreine hydrochloride. The puncture is made in the intercostal space over the focus of empyema with a needle of 1.5 mm. caliber which is connected to an aspirating syringe. Aspiration of pus is followed by intrapleural injection of filtered air in the proportion of half the amount of pus removed. The treatment is repeated to obtain complete elimination of pus. In no case is more than 200 cc. of air administered. After removal of pus, the pleural cavity is washed by repeated injection and aspiration of a 0.5 per cent solution of ethylhydrocupreine. When the fluid used in the lavage comes clear, 10 or 20 cc. of the solution is injected, the needle removed and the opening of the puncture covered with either collodium or adhesive plaster. Air is injected only in the first treatment. The subsequent treatments consist only in intrapleural lavage and storage of 10 or 20 cc. of the fluid in the pleural cavity. The best results are obtained when the treatment begins at the end of the third week of evolution of the disease. The average number of treatments is seven, given every other day. However, if the condition of the patient improves the intervals between injections are prolonged or the treatment is discontinued as signs of recovery indicate. In the twenty-four cases reported by the author, the disease was a complication of pneumonia in the majority of cases and of either bronchopneumonia or bronchitis in a few cases. The author concludes that the method of intrapleural injections of air gives a high percentage of recoveries (twenty-two of twenty-four cases) and a low rate of mortality (two of twenty-four cases). It can be resorted to as either a preparatory or a complementary method for a surgical intervention (Cocchi). The average duration is eighteen days. The treatment is indicated in large, small, free and encysted forms of pleurisy in infants. It is of an easy technic, economical and well tolerated by infants.

Deutsche Zeitschrift für Chirurgie, Berlin

250: 543-704 (Aug. 1) 1938. Partial Index

- *The Problem of Exophthalmic Goiter. P. Sunder-Plassmann.—p. 543.
Extradural Cysts in Spinal Canal. O. Haffner.—p. 559.
Diagnosis of Tumors of the Sympathetic. W. Bufe.—p. 571.
Histogenesis of Osteopiktilosis. L. von Stubenrauch.—p. 586.
*Physiology and Pathology of the Thymsus. H. Adler.—p. 614.
Traumatic Luxation of a Chopart Joint. R. Nicole.—p. 650.

Exophthalmic Goiter.—Sunder-Plassmann demonstrated, in dissections on rabbits, that bilateral resection of the cervical sympathetic fibers leaves the finer nervous structures of the thyroid and its vessels largely intact. Microscopic studies of rabbits' thyroid, previously activated by the thyrotropic hormone, demonstrated the manner in which the terminal nervous reticulum comes in contact with the individual follicle cell both on its periphery and with its plasma. He had likewise observed in thyroids activated by thyrotropic hormone a simultaneous enlargement of the follicular cells and an increase in the size of the Schwann's bodies in the preterminal nervous plexus. The terminal reticulum derives from the reticulum of the nonmedullated neurofibrils of the preterminal plexus and constitutes with the latter a single biologic entity. The author further demonstrated that the vegetative nervous apparatus of the gland remained intact as long as the gland was capable of remaining "refractory" to the thyrotropic hormone. As soon, however, as the "refractory stage" was broken, the thyroid exhibited severe toxic damage particularly in the preterminal plexus and its Schwann's plasmodium. The simultaneous intraperitoneal injection of the thyrotropic hormone and foreign serum (hogs') produced, in a few days, definite toxic damage in the vegetative nervous system. The gland appears to have lost the capacity for resistance, as a result of which the liver interstitium, the liver parenchyma, the adrenals

and the myocardium exhibited severe damage. On the basis of research performed by the author's associates at the Pathologic Institute in the University of Munster, the author rejects the hypothesis of an "antithyrotropic hormone" or of a special "antithyrotropic substance." He assumes the existence of an antigen-antibody reaction due partly to the introduction of a protein so that the smallest amounts of thyroxine in the serum of the previously treated animals may assume significance, and partly to the alterations of the general reaction of the organism in which the vegetative nervous system plays an important part.

Physiology and Pathology of Thymus.—On the basis of a clinically observed case, Adler advances the possibility of causal relationship between hyperplasia of the thymus gland and myasthenia gravis. He demonstrated in dogs that the changes in the muscles in myasthenia are of a chemical nature, that they can be provoked by the hyperfunction of the thymus gland and that the action is to be regarded as the effect of internal secretion of the gland. The striking clinical contrast between myasthenia and myotonia suggests that the latter may likewise stand in causal relationship to the thymus. The frequency of a hyperplastic thymus in exophthalmic goiter suggests that the myasthenic reaction present in a considerable proportion of these cases is due to the hyperfunctioning thymus. The author suggests that the presence of a hyperfunctioning thymus be determined by testing for myasthenic muscle reaction before operating on the thyroid. He advances the theory of a hyperfunctioning thymus as the main cause of postoperative exophthalmic symptoms. It is for this reason that they have adopted in Sauerbruch's clinic the removal of the thymus in addition to strumectomy in the cases of exophthalmic goiter with positive myasthenic reaction.

Folia Haematologica, Leipzig

60: 145-328 (Nos. 2 and 3) 1938

- Relations of Human Reticuloocytes in Bone Marrow and in Peripheral Blood. Magdalena Ungricht.—p. 145.
Morphologic Studies on Physiology of Erythrocytes and of Genesis of Blood Platelets. R. G. E. Ulpts.—p. 205.
Contribution to Study of Hematocytology of Normal Guinea Pigs. A. Botzaris.—p. 222.
Investigations on Family with Hemolytic Constitution and Study of Hemolysis in Hypotonic Solutions of Sodium Chloride. M. Decker.—p. 231.
Dependence of Viscosity Values of Blood on Pressure. F. Frimberger.—p. 237.
*Studies on Bone Marrow in Typhoid: I. Erythropoiesis. Z. Galinowski.—p. 243.
Acute Myelosis and Agranulocytosis. P. G. Ahlberg and N. G. Norden-son.—p. 258.

Bone Marrow in Typhoid.—Galinowski studied the bone marrow in sixty-three patients with typhoid. The bone marrow was obtained from the sternum by means of Arinkin's method, the puncture being made at the level of the second intercostal space. The bone marrow was examined for the number of erythrocytes, the hemoglobin value, the color index, the percentage of reticuloocytes and the number of nucleated elements, with consideration of the proerythroblasts, the erythroblasts and the normoblasts with basochromatic, polychromatic and orthochromatic protoplasm. Simultaneously with the bone marrow, the blood was examined for the number of erythrocytes, leukocytes and thrombocytes, for the hemoglobin content, for the color index and for the percentage of reticuloocytes. In summarizing the results of his studies the author says that the number of nucleated erythrocytes per cubic millimeter of bone marrow varied between 1,222 and 33,764. He regards values up to 4,000 as below normal, that is as indication of a reduced erythropoiesis; values between 4,000 and 10,000 as normal, and the values above 10,000 as an indication of an increased erythropoiesis. The author arrived at this classification on the basis of studies on normal persons. Manifestations of increased proliferation of the erythroblastic tissues were observed in the majority of cases during the second and third stages of typhoid. In addition to the duration of the disease, the severity of the course and the complications seem to play a part here. In convalescents and during remissions, the bone marrow usually is in a quiescent state. In the cases in which there was a normal number of erythrocytes in the blood, the activity of the bone marrow was either normal or showed signs of compensatory

activity. In cases in which symptoms of anemia were present, the behavior of the bone marrow was not uniform; in some cases there was no reaction at all, in others there was an erythroblastic hyperfunction and in still others there were signs of exhaustion. The latter were observed chiefly in the more severe degrees of anemia. During the second stage of the severe forms of typhoid and during its third stage in patients with complications, divergences were observed between the reductions of the erythrocyte count in the blood and in the bone marrow. The reticulocyte content of the bone marrow and even more so that of the peripheral blood did not always go parallel to the activity of the erythroblastic system. A simultaneous increase of the reticulocytes in the bone marrow and in the circulating blood was observed in those cases in which the bone marrow was rich in cells and the nucleated erythrocytes showed normal aspects. An isolated reticulocytosis of the bone marrow was frequently observed in connection with a deviation to the left of the nucleated erythrocytes. A stimulation of the erythropoiesis, relative to the leukoblastic system, to an extent that the nucleated erythrocytes amounted to from 25 to 40 per cent of all nucleated elements of the bone marrow, was usually observed during the third stage of the severe and complicated cases.

Zeitschrift für klinische Medizin, Berlin

134: 385-532 (July 6) 1938. Partial Index

- Symptomatology of Disorders Caused by Blood Transfusion (Gastro-Enteritis, Hypochloremia and Hemorrhagic Glomerular Nephritis as Result of Transfusion). G. Dinkler.—p. 385.
Multiple Myelomas and Leukemia. J. M. Nothoven van Goor.—p. 393.
Study of Surface Tension of Blood, Particularly in Renal Diseases. H. D. Ellenbeck.—p. 405.
*Behavior of Sodium/Chloride Index in Urine of Patients with Hepatic Disorders: Its Value in Diagnosis and Prognosis. H. W. Bansi and G. Strecker.—p. 410.
Pathogenesis and Therapy of Chronic Nephrosis. H. Reiners.—p. 429.
Clinical Electrocardiography: Type of Electrocardiogram in Obese Persons. G. Schlomka and H. Blanke.—p. 435.

Sodium/Chloride Index in Hepatic Disorders.—Bansi and Strecker studied the elimination of sodium and chloride and the sodium chloride index of the urine of patients with various hepatic disturbances. The studies were made on forty-two subjects: five normal persons, seven patients with cirrhosis of the liver, eleven with engorged liver, four each with catarrhal jaundice and with obstructive jaundice, three each with malignant tumors of the liver and with acute yellow atrophy of the liver, two with hemolytic jaundice and one each with arsphenamine jaundice, with gunma of the liver and with amyloidosis of the liver. In some of the patients the tests were continued for weeks. With one exception, all the subjects were free from renal disorders. They received a mixed diet, which usually had a low sodium chloride content, and 800 cc. of fluid. The authors say that the elimination of sodium and chloride and the sodium/chloride index are not to be considered as reliable tests for the function of the liver but rather as differential diagnostic and prognostic aids. They think that in diseases of the liver an index between 0.75 and 0.5 indicates a mild impairment, an index between 0.5 and 0.25 a moderate and an index below 0.25 a severe, usually fatal disorder. In cirrhosis of the liver, they observed a great reduction in the elimination of sodium and chloride and a reduction in the index. It was found that the lower the index, the more unfavorable was the prognosis. In carcinoma or in sarcomatous infiltration of the hepatic tissues, the sodium/chloride index as well as the sodium and chloride concentrations decrease as the destruction of the hepatic tissues progresses. In catarrhal jaundice the index decreases to below 0.5 until the height of the disease is reached, but during the period when the jaundice subsides the index rises to above 1 as the result of the elimination of large amounts of sodium. In obstructive jaundice the index values fluctuate considerably, but they remain within normal limits. If the index increases far above 1 in case of subnormal concentration in the urine, this is an indication of acute yellow atrophy of the liver if vomiting exists at the same time. However, an elevation of the index above 1 in the presence of a hypernormal concentration is to be found in the subsiding stage of catarrhal jaundice and during the elimination of edema in patients with heart disease.

Khirurgiya, Moscow

1-166 (No. 4) 1937. Partial Index

- *Tetanus: Passive and Active Immunization. I. G. Rufanov, Z. I. Mikhailova and I. A. Yatsевич.—p. 3.
Experimental Osteomyelitis. S. M. Derizhanov.—p. 16.
A Bleeding Wound as Desensibilizing Factor. O. N. Survillo.—p. 32.
Disinfection of Hands and Operative Field with Chlorated Ammonium in Alcohol. V. M. Vasilchuk.—p. 37.
Law of Localization of Metastases in Septicopycemia. V. A. Zhmur.—p. 43.
Streptocid Therapy of Erysipelas. M. S. Sokolov.—p. 52.
*Treatment of Purulent Gonitis. P. N. Napalkov.—p. 103.

Tetanus: Passive and Active Immunization.—On the basis of the review of the literature and their own clinical and laboratory investigations, Rufanov and his associates state that they do not see sufficient reason for rejecting the serum prophylaxis of tetanus. Despite the negative statements of Böhrer, they feel that serum prophylaxis has played an important part in reduction of the incidence of tetanus. The serum, however, should be administered as early as possible, preferably at the time of treatment of the trauma and, because of the rapid disappearance of the passive immunization produced by it, a secondary injection should be given after from seven to ten days, especially in the presence of a soiled wound. Among the shortcomings of passive immunization demonstrated by the authors in animal experiments they mention the short duration of immunity, a diminished effect with each subsequent immunization and the danger of serum disease. To obtain good results with the specific treatment, high doses of the antitetanic serum must be given. The clinical and animal researches of the authors confirm the results of Ramon of the Pasteur Institute as to the effectiveness of anatoxin for the purpose of active immunization against tetanus, its ability to increase rapidly the antitoxic titer after a considerable lapse of time and of complete safety of the method. Simultaneous administration of the serum and of the anatoxin, preferably in oil, constitute, by combining both the passive and the active immunization, the best prophylaxis against tetanus. For purposes of military hygiene the method may be simplified by combining it with vaccination against another infection, for example tetanus and typhus for adults, tetanus and diphtheria for children. The advantages of anatoxin are (1) its ability to lower the incidence of tetanus, (2) lessened danger of anaphylaxis and (3) the reduction of the expenses of serum prophylaxis and of treatment of tetanus.

Purulent Gonitis.—According to Napalkov, the primary and frequently the only method required in the treatment of purulent gonitis is immobilization of the limb, puncture and repeated flushing of the joint. Suppuration of the capsule or of the periarticular tissues requires an incision. Incision of soft tissues about the joint is preferable to initial arthrotomy. The author recommends the use of drains in arthrotomy only when incision is made in the joint capsule but not within the joint. The author limits the indications for resection in purulent gonitis to the initial phase of sepsis. Of the twenty-eight patients treated by the author on the conservative plan, twenty-three were cured and retained the limb. Two patients required amputation and three died.

Hospitalstidende, Copenhagen

81: 745-772 (Aug. 9) 1938

- Recent Investigations on Coagulation of Blood. T. Astrup.—p. 745.
*Comparison Between Changes in Electrocardiogram After Administration of Strophanthin, of Acetylcholine and After Irritation of Vagus. N. A. Nielsen and M. Trier.—p. 759.
Suspension of Uterus (Alex-Adams) in Operations for Prolapse Together with Review of Complete Prolapse Material from 1924 to 1933 (1934). A. Johnson and S. Müller.—p. 768.

Changes in Electrocardiogram.—Nielsen and Trier state that the changes in the electrocardiogram after the administration of strophanthin, after the administration of acetylcholine and after irritation of the vagus in the same person are identical: in bradycardia, relative shortening of the electric systole and, in case of marked bradycardia, changes in the T deflection in leads 1 and 2. This supports the assumption of acetylcholine as vagus substance and of sensitization of the heart musculature by strophanthin as due to the acetylcholine released by the normal vagus tonus.

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PREVENTIVE MEDICINE

ITS OUTLOOK IN MEDICAL EDUCATION

W. S. LEATHERS, M.D.

NASHVILLE, TENN.

Our ideas concerning the prevention and control of disease have undergone remarkable transformation during the past century and especially during the past fifty years. Many of the great conquests in medicine have been achieved in the field of preventive medicine and public health. One who reads the biographies of Walter Reed, Pasteur, Trudeau or "An American Doctor's Odyssey" by Heiser is impressed with the romance and spirit of adventure which one may experience in the prevention and control of disease and in the field of medical research. The progress that has been made in this phase of medical service constitutes a record of those principles the scientific application of which should ultimately result in "man's redemption of man."

CHANGING ATTITUDES TOWARD PUBLIC HEALTH

Before the era of the science of bacteriology and immunology the practice of preventive medicine was focused on the environment. The methods employed were based largely on empiricism. Our concept of preventive medicine at that time was completely dominated by the filth theory of disease. Public health procedures, as a consequence, were directed chiefly toward the abatement of nuisances, the removal of refuse, isolation and quarantine of the sick, and disinfection. This attitude toward public health prevailed largely until the epoch-making researches of Pasteur, Koch, Lister, Loeffler, Behring, Ehrlich, Laveran, Manson and Walter Reed, whose discoveries established the etiologic and immunologic factors involved in the use of scientific methods in the diagnosis, treatment and control of the infectious diseases. The emphasis that had been placed on the environmental theory of disease during the nineteenth century began to be discarded in favor of the germ theory at the beginning of the twentieth century. There was, therefore, a change in emphasis from the environmental factors of disease to the health of the individual himself and to his relation to the family and to the community. Thus our horizon was rapidly extended to include a study of maternal, infant and preschool care, the health of the school child, the effect of physical changes of adolescence on health, and the health problems of the adult and of the family

as the most stable unit of society. Periodic medical examination and general health supervision of the community likewise became of paramount importance in the public health program.

The "trial and error" method was gradually discontinued and the newer knowledge of preventive medicine was applied in a common sense, orderly and technical way. There have been organized, as a result, during the past twenty-five years an increased number of full time county or district health departments. These are usually directed by physicians whose professional education and experience are such as to command the respect and confidence of the medical profession and of the public. Experiments prove and experiences show that the methods of preventive medicine today may be considered as dependable as those of other branches of medicine. In reality, preventive medicine constitutes a part of clinical medicine, obstetrics, pediatrics and psychiatry, and even much of surgery. Its purpose is to avert those disorders for which there are specific preventive measures; to detect early by accurate and thorough methods of diagnosis the beginnings of illness for which remedial therapy may be effectively applied. Its objective is to aid in the solution of social, economic and welfare problems of the community in relation to disease. It involves the use of a special technic in dealing with the public. The application of the principles of preventive medicine through organized administrative procedure in relation to local, state and national needs constitutes public health. Obviously, preventive medicine and public health are complementary and interdependent. Each is indispensable to community welfare.

PROGRESS IN EUROPE

The question may be asked What is the present status of preventive medicine in medical education? In 1924, through the generosity of the Rockefeller Foundation, it was possible for me to devote a year in a study of medical education and public health activities in foreign countries. These were France, England, Scotland, Switzerland, Belgium, Germany, the Netherlands, Denmark and Norway. This investigation was undertaken with particular reference to the place of preventive medicine and public health in the scheme of medical education. It was a task of trying to determine what factors must be considered to provide adequate instruction in this subject, particularly for undergraduate medical students. Much time was devoted also to a study of public health administration and the facilities afforded for the professional education of public health personnel. In 1932 it was possible for me to return to Europe as a member of the Board of Scientific Directors of the International Health Division of the Rocke-

From the Department of Preventive Medicine and Public Health, Vanderbilt University School of Medicine.
Read before the Medical Section of the Inauguration Program of President Rufus Carrollton Harris, Tulane University, New Orleans, Jan. 17, 1938.

feller Foundation. This afforded an opportunity to extend these observations in other countries, namely Spain, Italy, Yugoslavia, Bulgaria, Austria, Poland and Hungary.

Significant progress had been made in many of these countries in the development and extension of organized public health work, largely as a result of the interest and grants-in-aid of the International Health Division of the Rockefeller Foundation.

The problems of medical education were of much interest, particularly in relation to the systems of medical service which had been developed in the older countries and which have been founded more largely on principles of state control than has been done in our own country. It was possible also to study the public health organizations and the methods that were employed in the protection of individual and community health. The interchange of points of view with public health authorities and teachers in medical faculties and official groups was helpful in forming a perspective with reference to the relationships which should be maintained in medical schools between the clinical branches of the curriculum and instruction in preventive medicine, and also the relationships which should exist between public health activities and the practice of medicine.

Time will not permit a more detailed consideration of this matter. It is sufficient to state that there was obvious need for more adequate instruction of medical students in hygiene and preventive medicine in the countries visited. The instruction in this phase of medical education was chiefly of a didactic nature. The courses consisted of from ten to seventy lectures, usually in the fifth curricular year and sometimes also in the sixth. Some attention was given to laboratory exercises with particular reference to water supplies, sewage products and food adulteration. Microbiology was included in the third year curriculum in a few medical schools. The lecturers or professors were frequently members of the local health service and therefore devoted a relatively small part of their time to teaching students. The teaching facilities in preventive medicine and public health were chiefly centered in institutions of hygiene and schools of public health in which there was a predominant interest in bacteriology and immunology, including clinical aspects of the infectious diseases. But little attention was given to administrative procedures in public health in relation to the practitioner of medicine and the technical phases of personal and community hygiene. There was, however, a marked interest in providing more adequate facilities for the teaching of undergraduate medical students.

Since 1932 more consideration has been given in these countries to the instruction of undergraduate medical students. This is particularly true of Cluj, in which a course of instruction for medical students is provided along modern lines, including reasonable opportunity for laboratory exercises and field demonstrations. The course consists of "instruction in the prevention of infectious diseases, disinfection, personal hygiene, housing, nutrition, water supplies, sewage disposal, child hygiene, industrial hygiene and vital statistics. The students are required to present before examination a sanitary survey of some village." The plan of instruction for medical students is also especially noteworthy and well developed in Nancy under the able direction of Professor Parisot. The teaching staff

of the Institute of Hygiene has a full time personnel which expresses consistent interest and constructive outlook in the plan of instruction of undergraduate medical students. Progress has been made also in Hungary, Poland, Czechoslovakia and Yugoslavia in this phase of instruction. There is a forward look in countries visited with reference to providing better facilities and more adequate instruction in hygiene and preventive medicine to undergraduate medical students. The training of the physicians in hygiene and public health should not be deferred as an interest in postgraduate instruction, which unfortunately has been done largely in many countries in developing public health organizations.

SITUATION IN THE UNITED STATES AND CANADA

Early in 1925 a few months were devoted to observations in the medical schools of some of the leading universities in the United States and Canada, notably, Harvard, Yale and the University of Toronto. The situation was obviously encouraging. Provision had been made for the teaching of preventive medicine and public health to medical students. The medical school in each of these universities had a reasonably well organized department provided with a budget and full time personnel for teaching and research. In Toronto the fifth year medical students devoted three weeks to field work in public health, one half of the class taking the work at the end of the session and the other half just prior to the beginning of the session of the sixth year. In Harvard, each medical student was required to make a careful sanitary survey before graduation in medicine as a part of the regular course in hygiene and preventive medicine. At Yale provision was made for a number of field demonstrations and special studies of public health activities in the municipal and state health organization. In these medical schools a serious effort was made to give the students some knowledge of personal and community hygiene and the application of preventive measures by official health agencies and their significance in relation to medical practice.

The outlook for preventive medicine in medical education in the United States is encouraging. However, if one is to realize fully the benefits that may be derived from the available knowledge for the control of disease and the promotion of individual and community health it is necessary that authorities in medical schools give intelligent and aggressive direction in effecting more adequate arrangements and facilities for instruction of students in this phase of medical service. No plan or system is offered for realizing this objective in medical education. The solution of the problem depends obviously on an analysis of the conditions confronting the medical faculty of each university. There can be, however, no question as to the need and the advisability of affording better facilities for this type of instruction in our medical schools.

In 1926 there were nine medical schools in the United States and three in Canada that had full time departments of preventive medicine. In each of these institutions a budget was provided and full time personnel was engaged in the instruction of undergraduate medical students. Today, with the criterion of the full time department as a basis for comparison, there are now approximately eighteen full time departments in medical schools in the United States and seven in Canada. This shows an increase in our own country of 100 per cent during the past decade and in Canada of slightly more

than 100 per cent. A few of the departments that existed in 1926 have enlarged their facilities for teaching and research. Much more emphasis is being placed also on the practical aspects of instruction such as assignments for field experience, field demonstrations, epidemiologic exercises, laboratory methods for the diagnosis of communicable diseases and environmental case studies. Special studies also are being made of public health problems in the community and state health organizations; seminars are being used as a means of developing the interpretative power of the student in statistical analysis and epidemiologic observations.

INSTRUCTION

Although the didactic or lecture method should be used, within limitations, in teaching preventive medicine and public health to the medical student, practical or clinical measures must be employed to gain and maintain the interest and stimulate the imagination of the student. The plan of teaching should give the student an experience reasonably comparable to that which is afforded by the "clinical clerkship" in medicine. For example, the environmental case study is a phase of instruction which is now used in Yale, Vanderbilt, Syracuse, Johns Hopkins and possibly other universities. This directs the interest of the student especially to the individual rather than to a group of the population. A particular clinical and public health problem is undertaken in the study of the patient in relation to his family, his home, his occupation, his social-economic status and to the official and unofficial health and welfare agencies whose aid may be invoked in the solution of the treatment involved. These cases are selected cooperatively by the clinical and public health departments and the social service division of the hospital. A report is finally made by the student to the class, and representatives of the agencies concerned are invited to attend. This method of teaching affords an unusual opportunity for the student to obtain some idea of the background of disease, its significance in the economy of life and the factors that should be considered in attaining the best results in the treatment of both the patient and the disease. The students display much interest in this type of teaching. Their imagination is stimulated by a clearer understanding of the social, religious, psychologic and economic factors involved in the effective use of therapeutic and preventive measures in the control of disease.

There is need to implement the practical aspects of instruction of medical students in preventive medicine and public health. The use of procedures which will integrate this instruction with other subjects in the medical curriculum is of the greatest value. A unified purpose should be created and maintained in the faculty for teaching the principles involved in personal and community health. The student must be aroused to have the long range view in the prevention and cure of disease. This objective cannot be successfully accomplished without a full time department of preventive medicine and public health which functions not only in giving necessary formal instruction to the students but which will also relate its work to the personnel of other departments in the medical school. This serves to stimulate and maintain the interest and cooperation of members of the faculty in establishing a point of view in the medical student which will cause him later to practice preventive as well as curative medicine. In a word, unless the instruction in this field of medical

service is organized so as to carry on a well ordered, effective and dynamic teaching and research program, the interest and imagination of the undergraduate medical student will not be secured and maintained comparable to that afforded by instruction in the fundamental sciences and the clinical branches of medicine. In schools where this is accomplished, gratifying results are obtained from the point of view both of training future practitioners in the preventive aspects of medicine and of causing a larger percentage of graduates to adopt public health as a career.

Preventive medicine and public health must be integrated in the scheme of medical education so that the 5,000 graduates of medicine who are turned out annually on a receptive public will be imbued with their responsibility to use in practice available knowledge for the prevention of disease and the protection of community health, for the physician in a sense should act the part of a deputy health officer. He should have an intelligent understanding of the activities of official and unofficial health agencies in his community and state. He should cooperate in promoting the work of the local health department. He should serve as an outpost in a field of preventive medicine. He should regard himself as an integral part of the national public health program.

If this goal is achieved a great and permanent contribution will be made in providing a more adequate medical service for the indigent and the low income groups of the population. There will also be a better understanding and, as a result, a closer cooperation between public health agencies, official and nonofficial, and the medical profession in the treatment and prevention of disease and, broadly speaking, in the general promotion of public health.

What motivating agencies are engaged to accomplish this result? From about 1920 the Association of American Medical Colleges and the Council on Medical Education and Hospitals of the American Medical Association have emphasized the great need for teaching preventive medicine and public health in the curriculum in the modern medical school. The records of the Association of American Medical Colleges show that provision was made in the constitution and by-laws published in 1907 in which thirty lectures were advised. However, in 1923, after a careful survey by a committee of this association, it was specified that from 3 to 4 per cent of the total number of hours (from 3,600 to 4,400) should be devoted to this type of instruction. This would mean approximately from 108 to 175 hours per year. In the *Proceedings of the Annual Congress on Medical Education and Licensure* of the American Medical Association a number of papers on this subject have been published during the past two decades concerning its place in the medical curriculum, and there appears to be an agreement between the two associations as to the minimum number of hours that should be included.

INSPECTION OF MEDICAL SCHOOLS

During a period of two years prior to May 1936, all the medical schools in the United States and Canada were inspected under the general direction of the Council on Medical Education and Hospitals of the American Medical Association. These data have been used in an attempt to evaluate the departmental activities, certain criteria being used that may be applied on a comparable basis. The Secretary of the Council on Medical Education and Hospitals in making his annual

report to the House of Delegates of the American Medical Association at its meeting in Atlantic City on June 7, 1937, made the following significant statement:

Preventive medicine, although of undoubted importance, has not yet developed a clearcut and generally accepted objective so far as the teaching of undergraduate medical students is concerned. In some instances a good deal of time is spent in demonstrating the activities of a state or city department of health; in others, students are required to make and report on a sanitary survey, while still others act on the assumption that for the man in practice the most important thing is that all of his daily contacts should be measured with a realization of the importance of prevention and that his attitude can be instilled only by clinical teachers who exemplify it in their own practice. A further study of this problem is an obvious need.¹

The chief difficulty, as I understand the problem, is not a question of an ill defined objective but rather a lack of available funds and the barrier afforded too often by the conservatism of medical faculties in making necessary adjustments in the curriculum for systematic instruction in the preventive and public health aspects of medicine. There appears to be a tradition of temporizing and in some instances of assuming a laissez-faire attitude in making adequate provision for this type of instruction.

WORK BEING DONE

Within recent years the Committee on Professional Education of the American Public Health Association, although organized primarily for the purpose of defining the professional educational qualifications of public health personnel, has also taken steps to stimulate interest in a more thorough preparation of the undergraduate medical student in the prevention and control of disease. A subcommittee has been appointed for this purpose and its chairman, Dr. W. G. Smillie,² on behalf of the committee, a few years ago enlisted the aid of Dr. Alan Gregg, director of the Division of Medical Sciences of the Rockefeller Foundation, in giving leadership in this undertaking. The first step was to provide opportunity for full time teachers of preventive medicine and public health to visit medical schools in which the instruction in this field was being done in a reasonably effective way. This afforded a basis for observation and interchange of experiences between members of medical faculties concerning this problem. Each person who was accorded this privilege was required to make a report embodying his observations and conclusions. Then a second step was taken, making it possible for several deans of medical schools to visit institutions in which there were full time departments of preventive medicine and public health. This proved stimulating and I hope constructive. The third step has been taken in securing the services of Dr. J. G. FitzGerald, professor of hygiene and preventive medicine in the Faculty of Medicine of the University of Toronto, and to assist him, Dr. C. E. Smith of Stanford University, to devote a year in a study of this problem in European countries and in the United States and Canada. This study was concluded in September 1937. Dr. FitzGerald will present his observations and conclusions at the annual meeting of the Council on Medical Education and Hospitals on February 14 in

Chicago. A summary of this information will be available for those who may be interested.

The Commonwealth Fund³ has provided during the past several years grants-in-aid for three medical schools—Vanderbilt, Tufts and Tulane—to enlarge their personnel and physical facilities for the instruction of medical students in the preventive and public health aspects of medicine. At Vanderbilt, a department of preventive medicine and public health was established on a full time basis when the medical school was reorganized in 1925. The curriculum is clearly oriented toward public health practice, although the teaching is effectively integrated with clinical instruction. At Tufts a strongly clinical slant has been developed in the instruction of the department, although some consideration is given to the public health aspects of this subject. At Tulane, although the broader aspects of public health are given consideration, the department of preventive medicine is essentially a clinical approach built round a rather broadly conceived periodic health examination plan of instruction. In all three departments the methods are somewhat different, but the objective has been maintained to secure, if possible, the interest of the student and to afford him opportunity to acquire information that may be used in the practice of his profession. The purpose of the fund was to introduce experimental procedures in determining effective methods which may be employed to improve the quality of instruction in preventive medicine and public health and to integrate more definitely the teaching with clinical branches of medicine.⁴

The outlook of public health in medical education and in practice was greatly facilitated by the passage of the Social Security Act by Congress in 1935. That act provides \$10,000,000 a year for use by the United States Public Health Service, on a diminishing scale during a ten year period, for the expansion of state and local health services. The fund is distributed (1) on the basis of population, (2) because of special health problems and (3) according to the financial needs of the respective states. As much as \$2,000,000 of the amount may be used for research. The money cannot be used to supplant existing appropriations of state and local health agencies but rather to stimulate additional appropriations and to provide for their most effective use. One of the purposes of the allocation of fund to the respective states is to provide competent personnel so as to raise the professional level of those who are to participate in the public health program. To meet this need a little more than \$1,000,000 has been set aside to provide subventions for developing postgraduate instruction in five universities, which are strategically located and in which facilities can be readily made available for this purpose. Postgraduate courses in five universities, from three to four months in duration, have been developed to meet an emergency need. In addition, the two schools of hygiene and public health at Johns Hopkins and Harvard universities have special endowments and facilities for graduate instruction in preventive medicine and public health. A number of other universities provide advanced instruction in public health as a part of the curriculum of graduate schools. For all practical purposes in some of these universities the opportunity afforded may be considered adequate in giving higher degrees such as that of Doctor of Public Health.

1. Cutter, W. D.: Report of the Council on Medical Education and Hospitals: Proceedings of the Eighty-Eighth Annual Session of the American Medical Association, J. A. M. A. 108:2134-2137 (June 19) 1937.

2. Smillie, W. G.: The Incorporation of the Principles of Preventive Medicine in Clinical Teaching, Proc. Ann. Cong. M. Educ., 1934, pp. 24-28.

3. Contributions to Professional Education, Annual Report of the Commonwealth Fund, 1936, pp. 18-24.

4. Annual Report of the Commonwealth Fund, 1936.

There are also being developed special health centers in New York City, domiciled in new buildings with improved facilities, five of which are located in districts in the environment of medical schools. These centers are to be used not only for the administration of public health in these areas but also for teaching undergraduate medical students and for training public health personnel. This opportunity is not limited to public health personnel employed by the city health department, but opportunity will be afforded for registration of those who may be engaged in public health work in other parts of the country. This is an advance step and one which gives increased recognition to the value of making adequate provision for teaching especially the medical student. Each of these medical schools will have a full time department of preventive medicine and public health and will be provided with adequate facilities for teaching in cooperation with the health centers.

There is a nationwide plan to provide full time, efficient public health service to every community in the United States. Obviously, the program that has been projected has created a great need for properly prepared physicians to engage in public health. It places a definite and immediate responsibility on the medical schools of this country to prepare their students in such a manner that a reasonable proportion of them will not only be attracted to public health as a career but be trained to integrate properly the preventive and clinical phases of medicine in special and general practice.

RESPONSIBILITY OF MEDICAL PROFESSION

It is clear, therefore, that the boundaries of the medical horizon are being rapidly extended because of new knowledge that is available for the protection of individual and community health. Moreover, the responsibility of the medical profession has been increased greatly because of the demands of the thoughtful public for improvement in the diagnosis, treatment and prevention of disease. This concept has been well expressed by Dr. Gregg⁵ in an address which he delivered during the Tercentenary Celebration of Harvard University Sept. 15, 1936, in which he stated:

The earliest intimation of the ultimate boundaries of medicine are beautifully outlined in the words of Christ, "I am come that they might have life and have it more abundantly." From the study of human genetics, and of nutrition, from the study of the human being as an indivisible unity, from grave consciousness of our obligations to society, and no doubt from unforeseen quarters will come knowledge that may make it possible not only to free the single life from much disharmony and disease, but to improve the stock and quality of human beings. Thus the very nature and future of man may become imperceptibly the great responsibility of medicine.

The implications are clear as to the place of preventive medicine and public health in fulfilling the increasing obligations and the high purpose of the physician in medical practice and in research.

5. Gregg, Alan: The Future of Medicine, Harvard Medical Alumni Bulletin, October 1936.

Forms of State Care for the Insane.—At present (1937), some twenty-four states operate under well defined systems of state care. The county care plan is in practice in a few states, notably Wisconsin, Pennsylvania, Iowa and New Jersey. In still other states, no definite plan of public provision for the mentally ill has been formulated.—Deutsch, Albert: The Mentally Ill in America, New York, Doubleday, Doran & Co., Inc., 1937.

OCCUPATIONAL DERMATOSES

AN EDUCATIONAL PROGRAM

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Diseases of the skin due to occupation represent from 10 to 12 per cent of all disease of the skin according to the best statistics available. They account for approximately 65 per cent of all disease due to occupational factors excluding industrial accidents. They cause considerable disability, usually partial but often complete. Such disability in most cases is temporary, but it must not be forgotten that sometimes it is permanent. Many thousands of dollars are lost in wages, and in addition large sums are paid for compensation and also for medical expenses.

Many diverse occupations are affected. Many cases are not recognized as possibly industrial until a considerable time has elapsed after the onset, and still more cases are not handled properly as industrial cases from the outset. In many the dermatosis is preventable, and often much can be done to lessen the disability. The preventive aspects of these diseases therefore need much more emphasis.

For these reasons, and perhaps others, considerably more publicity needs to be developed concerning occupational dermatoses. Much more information about their occurrence, causes, diagnosis, treatment and, especially, prevention needs to be presented to various groups over the country. In the first place, the public at large should be supplied with more information about this subject, perhaps by means of newspapers, magazines, including *Hygeia*, and public lectures. Workers of various classes, particularly of the occupations with the greatest hazards, need more instruction. Such instruction should be provided by employers with the help of insurance companies and safety engineering groups. Labor organizations, state boards of labor and hygiene and even federal agencies are doing much to make such material available for the worker. Employers too need awakening with reference to their responsibilities concerning this particular group of diseases, and various agencies could be called on to assist in their education. Insurance companies, better business bureaus, safety engineering associations and trade groups representing a particular industry are in a position to develop the facts for employers. The safety engineers are probably more awake to the problems than any other group, and their association, I believe, has the preventive phases at heart perhaps more than any other of the groups concerned.

Undergraduate medical students have comparatively little contact with such cases, and dermatologic courses in medical schools should of course include somewhat more about the occurrence, symptoms and prevention of the various industrial dermatoses that practitioners of medicine might have at their command more information about diseases of this type. Industrial nurses as a rule take over a factory position without a great deal of training in the subject but eventually develop by experience a good technic in their handling of cases which occur in their particular factory. A well trained industrial nurse can be a very efficient agent in the preventive management of industrial dermatologic con-

Read before the Section on Dermatology and Syphilology at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 15, 1938.

ditions, and courses in factory nursing should be developed in more centers throughout the country.

The members of the medical profession as a whole should have further information about occupational dermatologic conditions and should have their attention drawn to the frequency and to the various manifestations of these conditions. General practitioners, with their relatively limited experience with dermatologic conditions have not infrequently accepted erythema multiforme, scabies, lichen planus or even herpes zoster of the arm as of occupational origin. Some of these physicians may be performing part time industrial work in a neighborhood factory or shop and need considerably more information about the hazards and the manifestations which are possibilities in their particular industry. Full time industrial physicians have far more to do with industrial accidents, especially in view of the relatively small number of industrial diseases which occur in comparison with the accidents. While dermatologic conditions represent a major portion of the diseases, they may not occur with sufficient frequency, and the physician's knowledge of or interest in dermatologic conditions may not be sufficient, for him to estimate accurately the various cases as they occur. Courses should be available for these men to review their knowledge of dermatoses and their relationship to industrial processes. Dermatologists too are frequently not interested in the occupational phase. Their knowledge of processes and hazards is as a rule hardly sufficient for a correct classification of many cases as they occur. For industrial physicians, therefore, there should be evolved some plan of providing more data about the manifestations and about the processes in industry which may produce these manifestations.

Insurance companies, in many instances, are interested in keeping their claims as low as possible and frequently depend on general practitioners for a final diagnosis. They frequently delay consultation with a physician experienced in dermatologic conditions and trust that the patient's condition will clear up in time. With the insurance companies too the great preponderance of industrial accidents over industrial diseases makes it imperative that more attention be paid to them than to the diseases, with their smaller percentage of disability, yet these diseases, as a preventable condition, should receive more consideration. Most of the companies, however, do appoint capable specialists for the diagnosis of dermatologic manifestations and for advice with reference to treatment and the proper course to pursue in handling the cases.

Industrial accident procedure in various states differs greatly. It is too much to suppose that there will ever be a uniform procedure in all the states, but it is possible that greater publicity about the dermatologic phase of occupational claims would result in a greater degree of uniformity.

The groups which have been mentioned all need education: education with reference to the facts as they develop, education with reference to the possibilities of solving the problems outlined and particularly education with reference to preventive aspects. For the present, however, it is my purpose to discuss in more detail the matter of postgraduate medical training and teaching with regard to occupational dermatoses. I believe that such training or such teaching can be offered only in the larger cities, where there can be a definite coordination of all the organizations having an interest in these diseases. A definite central coordinating agency

is necessary, but whether this is a graduate school, a hospital or a group of interested physicians makes little difference.

For postgraduate medical training, however, certain aids are indispensable for the providing of adequate instruction. In the first place, there should be facilities for demonstrating occupational dermatoses such as can be furnished only by a comparatively large dermatologic clinic, by the dermatologic clinics of several large hospitals or by cooperation with the clinics maintained by various large insurance companies. There also need to be available good library facilities for the reading and reference work which is necessary for providing adequate information. Facilities for investigation of causal factors and preventive methods should be made available. Opportunities should be developed for visits to factories and shops where there can be seen under proper guidance, perhaps of both a factory official and a physician, the details of those processes which have the highest potential hazards to the skin. There should be enlisted the cooperation of insurance companies, industrial accident commissions and state departments of labor and hygiene so that every aspect of the situation may be covered. Lectures and conferences should be utilized to cover the most important phases of these conditions, and adequate lists of references should be provided for the use of the students.

The subject matter for these conferences might well vary widely in different sections of the country, possibly with reference to the particular problems of a locality or perhaps with reference to the persons presenting themselves for instruction. For general practitioners and industrial physicians greater emphasis could well be placed on the recognition of dermatoses in general, as well as on the industrial and legal aspects. For dermatologists, there could well be less emphasis placed on dermatologic earmarks and greater emphasis on the processes involved and the insurance and legal phases of these conditions. It is quite necessary that there should be outlined at the very start, so far as humanly possible, criteria which can be accepted for the diagnosis of industrial dermatoses, as well as criteria for the cure of such conditions. These problems are not settled, by any means, but I believe that continual emphasis on them will contribute very largely to the eventual settlement of these most trying definitions. There needs to be emphasis in these conferences on occurrence and causal factors, as well as on the occupations which are affected. Possible manifestations and the different types of disease involved, as well as the differential diagnosis, need emphasis. As I have said before, there is needed not only diagnosis of the condition but so far as possible a diagnosis of the causal factor. Treatment and special prevention call for thorough discussion and a familiarity with studies which have been made in the past and the effect which such studies may have on the matter of prevention. The possible relationship of allergy, of syphilis and of fungous infections is sufficiently important to require detailed consideration. There is much information available with regard to trades and processes, and in the inspection of such processes in factory visits considerable attention should be paid to the details of the preventive measures which have been developed. When one comes to the consideration of compensation acts and the insurance aspects of the subject there is much material to be considered in these conferences.

It will help if these subjects can be discussed from the point of view of the insurance official, perhaps a claim adjuster, perhaps a safety engineer, perhaps a full time industrial physician. It may help to have a discussion of the loss of time, compensation, wages and medical expenses and the possibility of lessening these items by more attention to the subject of prevention. The mere fact of discussion by a member of a state compensation board, an official of the state department of labor and a representative of industry will bring to the speaker's mind, as well as to the minds of the listeners, the fact that the subject is a live one and of interest to others and will aid in concentrating attention on an important subject for consideration.

The work of the dermatoses investigation office of the National Institute of Health, maintained in New York City under the direction of Dr. Louis Schwartz, should be reviewed in some detail. The work which is being done by this office in the investigation of dermatologic hazards in industrial processes over a wide area deserves commendation. This office receives requests for information from many sources, abstracts and indexes available literature on occupational dermatoses, arranges for chemical or other examination and sends out information to manufacturers, insurance companies, physicians and others. Such work deserves extension in order that puzzling problems which are continually arising among workers with potential hazards may be investigated properly and an attempt at settlement made.

Such in brief are some of the subjects on which attention should be focused when postgraduate instruction is being provided for those physicians who come in contact with dermatoses of possible occupational origin.

Under the auspices of the Harvard School of Public Health there has been started a course based on such an outline. The course is planned to occupy one month and will be conducted through the cooperation of various agencies and under the direction of the assistant dean of the public health school. It is arranged that two mornings a week will be devoted to factory visits in industries with potential dermatologic hazards, and two mornings a week will be spent in lectures and conferences. Members will spend one morning in the outpatient dermatologic department of a large hospital observing, particularly, cases of possible occupational origin and some of the more common dermatoses to be reviewed, as well as the various manifestations of disease caused by fungi. One morning a week will be spent either with the state department of occupational hygiene in the investigation of possible dermatologic cases or in hearings of the industrial accident board to view the procedure of this board. Through the cooperation of various insurance companies three or four afternoons a week will be devoted to the observation of industrial dermatoses as seen in their clinics, and one afternoon will be devoted to library work on references and required reading for the course.

Such a program not only indicates the benefits to be derived from the cooperation of interested agencies but should provide much needed information for persons desirous of obtaining a wider knowledge of occupational dermatoses. It is reasonable to suppose that these diseases are bound to assume a greater importance in preventive medicine as time advances, and the medical profession should be prepared to assume the burden of providing adequate instruction in this branch.

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THE INCIDENCE OF OCCUPATIONAL DERMATOSES AND THEIR CAUSES IN THE BASIC INDUSTRIES

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Of prime importance in the effort to control occupational dermatoses is the knowledge of their incidence and causes. Statistics on this subject have been compiled for many years in certain European countries. In the United States until four years ago such statistics were available only from nine states. Since then, however, there has been a marked increase of interest in this subject, and this year there are twenty-five states which gather statistics and have laws that compensate workers for disabling occupational dermatoses.

INCIDENCE IN EUROPEAN COUNTRIES

In England between 1921 and 1929 there was an annual average of 769 cases of compensated occupational dermatosis, or about 56 per cent of all occupational diseases. In the three year period of 1930 to 1932 inclusive there was an annual average of 1,368 cases of occupational dermatosis, or about 72 per cent of all occupational diseases.¹ In 1936 there were 1,771 cases of occupational dermatosis with an additional 142 cases of occupational epithelioma and eighty-four cases of chrome ulceration.² All other occupational diseases compensated in 1936 totaled 428 cases.

The three chief responsible agents were oils, alkalis and friction and heat, and the largest number of persons affected were engineers.

It is stated by English writers that these figures do not represent the actual incidence of occupational dermatoses, because only those cases in which the incapacitation is for one week or more and in which compensation is paid are reported. White³ estimated that at least from eighteen to nineteen thousand cases occurred in England each year.

The yearly incidence of occupational dermatoses in Germany is not available, but in 1935 the number of reported cases of occupational diseases, not including dermatoses, was 8,601.⁴ Of this number, 2,137 were in the metal industries.

There are no complete statistics from Italy, but Levi⁵ found fifty cases of occupational dermatosis among 1,156 workers in a period of six months, or an annual rate of 9 per cent.

INCIDENCE OF OCCUPATIONAL DERMATOSES IN THE UNITED STATES

In 1933 the nine states which kept records reported 5,787 cases of compensated occupational dermatosis in a total of 8,875 cases of occupational disease, or about 65 per cent.

The latest available records from five of these states show that occupational dermatoses are increasing and

Read before the Section on Dermatology and Syphilology at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 15, 1938.

1. International Labour Office: Occupation and Health, Geneva, League of Nations, 1930, vol. 2, p. 861.

2. Gafaer, W. M.: Occupational Diseases Occurring in Factories and Workshops of Great Britain in 1936, Pub. Health Rep. 52: 1303-1307 (Sept. 17) 1937.

3. White, R. Prosser: The Dermatogoses, ed. 3, London, H. K. Lewis & Co., Ltd., 1928, p. 9.

4. Berlin Letter, J. A. M. A. 108: 741-742 (Feb. 27) 1937.

5. Levi, Italo: Considerazioni sugli eczemi professionali, Dermosiflografo 12: 1-37 (Jan.) 1937; abstr. Zentralbl. f. Haut. u. Geschlechtskr. 57: 52-53 (Jan. 20) 1938.

other occupational diseases are decreasing, so that occupational dermatoses now comprise about 70 per cent of all occupational diseases, as shown by table 1.

THE PROPORTION OF OCCUPATIONAL DERMATOSES
TO ALL DERMATOSES

Many variable factors enter into the different estimates, the chief ones being (1) the percentage of the industrial workers to the general population and the prevailing types of industry in the localities where the estimates are made and (2) the criteria used in arriving at a diagnosis.

TABLE 1.—Incidence of Occupational Dermatoses in
Five States

State	Year	Occupational Diseases	Dermatoses	Year	Occupational Diseases	Dermatoses
Connecticut.....	1933	557	388	1936	411	249
Massachusetts.....	1932	954	613	1936	755	584
New Jersey.....	1933	468	352	1936	418	283
Ohio.....	1931	1,582	902	1936	1,500	1,092
New York.....	1931	1,012	610	1937	1,764	1,125
Total.....		4,573	2,944		4,848	3,343

Fordyce⁶ stated that occupational dermatoses are 2 per cent of all dermatoses. Lane⁷ stated that they comprise from 4 to 5 per cent. White⁸ gave the figure as 6 per cent. Gardiner⁹ gave it as 7.5 per cent, and Knowles⁹ estimated it at 10 per cent. Oppenheim¹⁰ estimated that 20 per cent of all dermatosis is of occupational origin and stated that occupational eczema is the most frequent of all diseases of the skin.

In studies of the United States Public Health Service of records in New York free clinics in 1930, only fifty-eight cases in which the diagnosis was occupational dermatosis were found among 25,000 new cases of dermatosis. This is a very low percentage and may be due to the fact that the occupational histories of the patients were not carefully taken and patch tests were but seldom performed. Many cases of occupational dermatosis were probably lost in the large number in which a diagnosis of eczema or dermatophytosis was made.

A more accurate conception of the prevalence of occupational dermatoses can be obtained by studying their occurrence in various industries. The Public Health Service made studies among more than 100,000 workers in various factories and found that in the period of a year about 1 per cent of all workers in these factories were affected with occupational dermatoses. These figures do not include burns, splashes of acids or alkalis or pyogenic infections of occupational cutaneous wounds, which affected about 10 per cent of 72,000 workers in an automobile factory and about 10 per cent of 2,500 workers in a chemical and dye factory.

Because the workers in the industries listed are seemingly exposed to contact with strong alkalis, acids, solvents and oils, one would expect to find a larger percentage of occupational dermatoses among them than among workers in trades in which such primary irritants are not handled. Yet this is not necessarily true, because in most of the factories there are safety devices such as enclosed processes and forced ventila-

tion which minimize the possibility of contact, and it will later be shown that just as many cases of occupational dermatosis are reported to occur among the workers in the domestic service, personal service and food-handling trades. Therefore it is conservative to estimate that 1 per cent of the industrial workers in the United States (not including clerical workers) are annually affected with occupational dermatoses.

CAUSES OF OCCUPATIONAL DERMATOSES

The predisposing causes of occupational dermatoses are personal and environmental factors which impair the defense mechanism of the skin against external irritants. They are:

1. *Race*.—Race is a predisposing cause, as it has an anatomic and physiologic effect on the skin. It is well known among workers that Negroes and brunets are less susceptible to irritants of the skin than blonds. For this reason many factories will employ only Negro or dark-skinned workers for jobs in which there is exposure to irritant chemicals. Workers with dark, thick, oily skin, like that of the Latin races, will withstand the action of such chemicals as soaps, turpentine and the volatile solvents better than workers with the dry skin. Workers with much hair on the legs and arms are more apt to acquire folliculitis from oils, grease and dirt than those with comparatively hairless skin. Workers with excessive sebaceous secretions are more likely to have occupational acne when exposed to chemicals and waxes.

2. *Perspiration*.—The perspiration normally acts as a mechanical remover and diluent of irritants coming in contact with the skin, but excessive perspiration, especially when combined with friction, may of itself irritate and macerate the skin and impair its resistance to irritants. Moreover, excessive perspiration may furnish the moisture necessary to make certain solid chemicals irritants, for instance by converting calcium oxide into slaked lime. The pH of the perspiration affects

TABLE 2.—Yearly Prevalence of Occupational
Dermatoses by Industries

Industry	Number of Workers	Number of Cases of Dermatoses	Percent
Fabric dyeing	3,800	76	2.0
Fur dyeing	1,000	17	1.0
Rubber manufacture	8,000	84	3.0
Oil refining	14,000	473	3.0
Candy manufacture	1,236	36	7.0
Chemicals and dye manufacture	2,600	176	7.5
Synthetic resin manufacture	700	53	2.0
Rayon manufacture	4,000	80	1.5
Steel manufacture	3,500	52	1.0
Glass manufacture	5,700	54	3.5
Tanning	565	20	0.4
Automobile manufacture	72,000	281	1.2
Totals.....	117,601	1,402	

solvent properties of chemicals and in this manner affects their action on the skin, because in order to be an irritant a solid chemical must be more or less soluble in the fluids of the skin.

3. *Diet*.—The food one eats plays a part in the predisposition to occupational dermatoses by affecting the pH of the perspiration and by affecting the relative proportions of calcium, magnesium, sodium and potassium in the skin. A high calcium-potassium ratio with an increase in the total calcium was shown to be present in cases of heightened sensitivity of the skin and the reverse in cases of lowered sensitivity.¹¹

11. Saito, Teichii: Jap. J. Dermat. & Urol. 33: 482 (May) 1934.

6. Fordyce, J. A.: Occupational Skin Diseases, J. A. M. A. 59: 2043 (Nov. 23) 1912.
7. Lane, Guy C.: Industrial Dermatoses at the Massachusetts General Hospital, Arch. Dermat. & Syph. 6: 565 (Nov. 1) 1922.
8. Gardiner, F.: Brit. J. Dermat. 34: 297 (Oct.) 1922.
9. Knowles, F. C.: Eczema of External Origin and Its Relationship to Dermatitis, J. A. M. A. 68: 79 (Jan. 13) 1917.
10. Oppenheim, M.: Transcript of the London Dermatological Society, 1924, pp. 51-74.

4. *Age*.—Most of the workers affected with acute eczematoid types of occupational dermatoses are either young or new at the job, while the chronic eczematoid types of occupational dermatoses occur mostly in older workers.

5. *Sex*.—The reports from compensation boards show more men affected by occupational dermatoses than women. This may be because women usually pay more attention to personal cleanliness than do men, because they are not exposed to strong irritants or because there are fewer women employed.

6. *Season of the Year.*—Occupational dermatoses are more prevalent in warm weather, when little clothing is worn and contact with irritants is more likely to occur, but in those industries in which the work clothes become saturated with irritants or dust filters through the clothing dermatoses may occur more frequently in the winter, because the men are less apt to take cleansing shower baths after work when the weather is cold.

7. *Other Dermatoses.*—The presence of other diseases of the skin, especially of the itching type, with scratching breaking the skin and tending to rub in any irritant deposited on it, also predispose to occupational dermatitis.

8. *Cleanliness*.—Lack of cleanliness is the most important predisposing cause of occupational dermatitis. Lack of cleanliness in the work environment is as important as lack of personal cleanliness. The daily cleaning of floors, walls and machines, combined with a daily change to clean work clothes and compulsory shower baths after work, will do much to lessen the occurrence of occupational dermatoses.

9. *Hypersensitivity*.—A frequent predisposing cause of occupational dermatoses is hypersensitivity, and impairments of the defense mechanism of the skin are the most frequent causes of hypersensitivity. The presence of other dermatoses, breaks in the skin and slight variations from the normal in the anatomic or physiologic aspect of the skin accounts for a large percentage of hypersensitivity.

10. *Allergy*.—Hypersensitivity in which an external chemical coming in contact with the skin or being absorbed into the body through other channels causes the formation of antibodies is not a frequent cause of occupational dermatoses. It is, however, a frequent cause of dermatoses occurring among the users of manufactured goods. In many cases occupational dermatosis seemingly due to allergy will be found by careful study to be due to physical changes in the skin of the worker, to changes in the working condition or to contact with a primary irritant.

ACTUAL CAUSES

Mechanical causes such as pressure, friction, abrasions and wounds are not in themselves frequent causes of occupational dermatoses, but they often open the skin to the action of chemicals and to bacterial infections.

Physical causes of occupational dermatoses are dry and wet heat causing burns and scalds; cold causing frost bite and chilblains; radium and roentgen rays causing burns and malignant changes in the skin of radiologists, and solar radiation causing sunburn, epithelial proliferations, melanosis and urticarial eruptions on the skin of some photosensitive open air workers.

Recent publications show that exposure to certain plants, perfumes and chemicals, especially those found in coal tar, renders the skin hypersensitive to solar radiation.

BIOLOGIC CAUSES

The biologic causes are not in themselves frequent primary causes of occupational dermatoses, but they do cause a large percentage of occupational dermatoses

TABLE 3.—Distribution of the 3,136 Cases for Which the Industry or Occupation of the Affected Person Was Unknown, According to the Specific Materials Constituting Each of the Twenty-Five Major Groups of Materials

	No. of Cases		No. of Cases
1. Acids and acid fumes.....	170	14. Halogens and their deriv- atives.....	11
Acetic acid or acetic acid fumes.....	4	Chlorine solution.....	9
Citric acid.....	1	Hydrofluoric acid.....	1
Fruit acids.....	8	Hydrofluosilicic acid.....	1
Hydrochloric acid.....	8	15. Metals and metal plating.....	340
Nitric acid.....	1	Aluminum.....	1
Oxalic acid.....	6	Mercury.....	297
Sulfuric acid.....	4	Metal polish.....	12
Vinegar.....	1	Nickel.....	6
Unknown or unspecified acids or acid fumes.....	137	Plating acid or solution.....	20
2. Alkalis and their com- pounds.....	498	Zinc.....	1
Ammonia.....	18	Metal unspecified.....	3
Calcium hydroxide.....	5	16. Nonmetallic elements.....	7
Caustic soda.....	90	Arsenic.....	3
Lime (calcium oxide).....	55	Sulfide.....	2
Lye.....	3	Sulfur dioxide.....	2
Soap and soap solutions.....	246	17. Oils—vegetable (oils, fats and waxes).....	4
Soda water.....	37	Oil—vegetable.....	4
Sodium carbonate.....	13	18. Paints, enamels and var- nishes.....	28
Sodium hydroxide.....	22	Lacquer.....	7
Sodium silicate.....	2	Lead paint.....	2
Alkali unspecified.....	7	Varnish.....	1
3. Biologic agents.....	35	Paint unspecified.....	18
Fruits and vegetables.....	2	19. Petroleum products and greases (mineral oils).....	220
Fungi.....	24	Cutting oils.....	34
Vegetables.....	9		1
4. Building cement and con- crete.....	45		9
Cement, unspecified.....	45		1
5. Burns and physical agents	42	Petroleum naphtha.....	3
Friction.....	13	Oil unspecified.....	138
Trauma.....	2	20. Plants.....	701
Physical agent unspeci- fied.....	27	Bulbs and flowers.....	5
6. Chemicals unspecified.....	60	Poison ivy.....	376
Chemical unspecified.....	60	Plant unspecified.....	320
7. Chromates and chromic acid.....	33	21. Resin.....	14
Chrome unspecified.....	34	Bakelite.....	4
8. Coal tar products.....	24	Metapora aminophenol.....	3
Cresosote.....	3	Resin unspecified.....	7
Naphthalene.....	10	22. Rubber and its compounds	54
Phenol, phenol oil and phenol products.....	11	Accelerators, catalyzers used in the rubber in- dustry.....	34
9. Cyanides.....	17	Aniline.....	34
Hydrocyanic acid.....	1	Accelerators, unspeci- fied.....	6
Potassium cyanide.....	4	Rubber cement.....	2
Sodium cyanide.....	1	Rubber unspecified.....	12
Cyanide unspecified.....	11	23. Solvents (other than min- eral oils).....	261
10. ".....	24	Alcohols—ethyl, methyl, wood.....	4
	16	Aminobenzene.....	20
	6	Benzene (benzol).....	4
	1	Benzine.....	10
	1	Carbon tetrachloride.....	2
11. Dusts.....	53	Cellulose acetate.....	1
Inorganic.....	1	Solution of formalde- hyde.....	11
Organic:		Gasoline.....	72
Cotton, felt.....	3	Hydroxybenzene.....	2
Flour dust.....	9	Kerosene.....	6
Leather dust.....	2	Nitrocellulose solvent.....	1
Spices.....	4	Shoe cleaner and polish.....	3
Starch.....	2	Shoe dressing.....	5
Wood dust.....	8	Silk washing solution.....	26
Organic dust unspecified.....	10	Thinner.....	1
Dust unspecified.....	14	Toluene.....	1
12. Dyes and dye intermedi- ates (fur dye not in- cluded).....	93		40
Cloth dyes.....	30		20
Ink.....	3	24. Miscellaneous.....	9
Leather dyes.....	5	Glue.....	4
Silk dyes.....	3	Medicines.....	3
Dye unspecified.....	52	Sugar.....	2
13. Furs and fur dyes, hides.....	47	25. Unknown.....	227
Fur dyes.....	43	Dermatitis unspecified.....	109
Furs.....	3	Infection.....	2
Paraphenylenediamine.....	1	Unknown.....	23

by secondary infection of occupational wounds and other cutaneous lesions. They are (1) bacteria, (2) fungi and (3) parasites.

The principal occupational bacterial infections of the skin are folliculitis, boils, bacterial infections of occu-

TABLE 4.—Incidence and Causes of Industrial Dermatoses Based on Cases Reported to the Division of Industrial Hygiene (Frequencies arranged in decreasing order of magnitude)

Industry or Occupation	Total, All Material Exposure	Petroleum Products and Greases	Solvents (Other than Mineral Oils)	Chromic Acid	Alkalis and Their Compounds	Metals and Metal Plating	Dusts	Chemicals, Unspecified	Dyes and Dye Intermediates (For Dye Not Included)	Plants	Rubber and Its Compounds	Building Cement and Concrete	Paints, Enamels and Varnishes	Synthetic Resins	Acids and Acid Salts	Burns and Physical Agents	Cyanides	Biologic Agents	Coal Tar Products	Furs and Fur Dyes, Hides	Nonmetallic Elements	Oils—Vegetable (Oils, Fats and Waxes)	Descalcifiers	Halogens and Their Derivatives	Miscellaneous	Unknown	
1. Metal industries (except iron and steel).....	5,480	539	574	445	431	386	632	219	936	277	169	183	170	130	142	101	58	21	74	56	46	37	30	6	114	137	
(a) Electroplaters, platers.....	530	68	52	205	19	186	4	14	21	2	32	4	48	4	1	1	1	42	
(b) Other metal workers, polishers, workers in metals unspecified.....	532	66	45	9	15	84	4	10	21	2	19	4	6	38	
2. Iron and steel industries.....	284	222	59	13	10	22	15	19	..	2	2	..	25	11	25	13	11	1	11	1	1	1	1	57	
3. Machine operators, machinists and machinists' helpers.....	556	325	34	15	16	22	19	12	1	3	1	24	9	10	2	2	11	1	10	4	24
4. Domestic and personal services.....	457	2	87	5	269	27	27	17	17	10	2	..	3	9	..	12	1	..	4	3	3	3	3	50	
(a) Cleaners, dish washers, maids, etc.; janitors; porters.....	335	2	48	5	180	7	17	17	17	10	2	..	3	9	..	10	1	..	4	3	3	3	3	49	
(b) Cleaning, dyeing, linens, linens at home or elsewhere.....	87	..	37	..	15	..	16	1	1	2	1	..	2	1	16	
(c) Barbers, beauty parlor employees, etc.....	45	..	2	1	12	16	
5. Food industries.....	347	6	10	2	34	5	60	8	41	1	1	14	7	..	21	3	7	18	..	42	70	
(a) Bakers, confectioners, cooks, salad makers, etc.....	133	5	4	..	11	5	20	5	..	3	1	16	7	..	21	3	7	18	..	42	70	
(b) Food handlers, grocery store and market workers, etc.....	129	1	3	..	4	2	9	3	2	11	3	3	21	..	26	35	
(c) Dairy and dairy products.....	49	..	3	..	17	..	1	1	3	14	30
(d) Fish or fish packing.....	16	2	..	1	1	3	2	9
6. Building and construction industries.....	305	19	46	12	8	6	18	17	2	36	8	14	37	1	5	6	1	..	3	..	4	..	2	..	2	27	
7. Cement, glass and pottery industries.....	287	19	14	3	19	1	25	5	1	169	1	..	3	2	1	..	2	1	1	10	
(a) Cement workers.....	175	4	17	1	31	3	169	1	..	3	2	2	1	1	1	
(b) Glass workers.....	94	14	10	..	2	1	4	
(c) Pottery workers.....	18	1	4	..	2	..	2	2	1	4	
8. Rubber industries.....	254	6	19	2	7	..	12	14	..	6	161	2	1	2	3	9	
(a) Clothing and textile industries.....	253	14	7	1	6	31	45	8	92	1	1	2	1	3	9	
(b) Clothing makers and manufacturers.....	106	13	4	1	1	2	25	6	73	1	4	3	1	40	
(c) Hosiery makers and manufacturers.....	45	..	1	1	29	1	6	34	
(d) Woolen mill workers.....	44	1	2	20	2	11	1	4	
(e) Mattress and rug makers.....	3	1	..	2	4	
9. Chemical industries.....	255	3	26	22	10	9	1	62	17	3	3	1	14	1	7	2	9	1	3	..	3	2	13	19
(a) Chemists, druggists, embalmers, laboratory workers, etc.....	116	1	7	13	5	4	..	41	3	2	1	1	14	1	5	2	9	1	3	..	3	2	13	19
(b) Dye manufacturers, paint and varnish manufacturers.....	51	2	15	2	1	2	1	41	3	2	1	1	14	1	5	2	9	1	3	..	3	2	13	19
(c) Bleaching, coloring, printing cloth.....	24	..	1	2	2	1	..	6	8	1	2	10	12
(d) Developing films, photography.....	22	..	3	3	9	8	1	4
(e) Fertilizer workers.....	17	1	2	3	1	1	1
(f) Extremities, insecticides.....	5	1	1
10. Leather and fur industries.....	220	1	30	6	4	..	43	14	51	1	12	1	2	2	1	1
(a) Leather and shoe workers.....	176	1	30	5	4	..	43	13	43	1	12	1	2	2	1	1
(b) Fur dyers, furriers, fur workers.....	44	1	1	1
11. Paper, printing and allied industries.....	206	3	25	46	4	13	8	20	42	2	1	6	1	2	1	1
(a) Blueprinters, embossers, etchers, lithographers, printers.....	165	3	20	46	4	13	8	20	42	2	1	6	1	2	1	1
(b) Binders, paper and paper goods manufacturers.....	41	..	5	3	8	10	1	1	1	1
12. Laborers.....	179	22	12	37	19	4	8	8	2	14	..	1	6	1	2	4	28
13. Transportation.....	103	48	62	1	11	3	4	6	1	5	2	1	5	1	2	9	9
14. Molders and workers in plastics (bakelite, etc.).....	116	..	8	1	..	1	12	104	1	3
15. Farmers, florists, gardeners, stock workers.....	105	..	1	1	71	1	3
16. Furniture industries.....	96	5	14	..	1	..	29	4	11	1	2	10
17. Clerical occupations.....	77	7	2	5	3	2	6	7	12	2	3	6	6
18. Highway and road workers, municipal workers.....	72	1	3	..	2	..	3	..	26	1	3	1	13
19. Seamen.....	42	6	5	4	2	4	2	0	1	13
20. Workers in electrical supplies and equipment.....	42	6	5	4	2	4	2	0	1	13
21. All others.....	171	48	53	65	11	16	42	26	18	30	3	1	35	2	14	15	9	15	24	6	14	6	6	2	2	17	97

* Industry unknown or not elsewhere specified.

* Inductive unknown or not elsewhere classified.

pational wounds, impetigo, erysipeloid, butcher's pemphigus, verruca necrogenica, vaccinia, anthrax and glanders. Of these, the first three are by far the most prevalent.

The principal fungi that cause occupational dermatitis are yeasts and *Monilia* in bakers and fruit and vegetable canners; *Tinea* in barbers, bath attendants and workers with animals or their hides, and *Sporotrichum*, *Blastomyces* and *Actinomyces* in horticulturists.

The principal parasites causing occupational dermatitis are *Pediculoides ventricosus*, causing grain itch; *Ancylostoma*, causing ground tich in miners, agriculturists and laborers; *Carpoglyptus passularum*, causing dermatitis among dried fruit handlers, and *Acarus sarcoptes* and *Demodex*, the parasites that cause mange in dogs and sometimes affects the skin of man.

CHEMICAL CAUSES

The chemicals, including plants, are the most frequent causes of occupational dermatoses.

Some of the states compile statistics showing the causes of occupational dermatoses among their workers and the industries in which they occur.

From 9,116 cases of occupational dermatosis reported to the Public Health Service from a number of states, tables have been compiled showing the causes of occupational dermatoses and the industries in which they occur.

Table 3 shows the causes in 3,136 cases in which the industry was not given. The principal causes in

TABLE 5.—Number and Percentage of Cases of Dermatitis by Major Material Classification; Cases Include Those with Industry or Occupation Known as Well as Unknown (Based on Tables 4 and 1)

Major Material Classification	Number	Percentage
Total, all classifications	9,116	100.0
Petroleum products and greases	1,068	11.7
Plants	978	10.7
Alkalis and their compounds	929	10.2
Solvents (other than mineral oils)	897	9.2
Metals and metal plating	726	8.0
Chromates and chromic acid	478	5.2
Dusts	435	4.8
Dyes and dye intermediates (fur dyes not included)	389	4.3
Chemical, unspecified	379	4.2
Acids and acid fumes	312	3.4
Rubber and its compounds	253	2.8
Building cement and concrete	231	2.5
Paints, enamels and varnishes	198	2.2
Resin	164	1.8
Burns and physical agents	143	1.6
Biologic agents	112	1.2
Cyanides	103	1.1
Furs and fur dyes, hides	103	1.1
Coal tar products	98	1.1
Desiccators	54	0.6
Nonmetallic elements	35	0.6
Oils—vegetable (oils, fats and waxes)	41	0.4
Halogens and their derivatives	17	0.2
Miscellaneous	123	1.3
Unknown	894	9.8

the order of frequency are plants, 22 per cent; alkalis, including building cements, 18 per cent; metals and metal plating, 11 per cent; solvents, 9 per cent; petroleum products, 7 per cent; dyes and dye intermediates, 4.5 per cent.

Table 4 contains an analysis of 5,980 cases according to industry and cause. The metal industries head the list, with over 30 per cent of all cases, and the domestic and food industries come second and third respectively. The building and construction industry comes next. In this industry the principal causes of dermatoses are the

alkaline cements and concretes. Next on the list are the cement, glass and pottery industries, and in this group more than 93 per cent of the persons affected are cement and glass makers, with the alkalis as the chief irritants. The rubber industry, which some years ago furnished a high percentage of occupational dermatoses, comes next. The precautions against occupational diseases which have been adopted in this industry of late years account for the great decrease of occupational dermatoses in it.

TABLE 6.—Causes of Dermatoses

Irritant	Number of Cases	Percentage
Alkalis	1,160	12.0
Petroleum products	1,068	11.0
Solvents	1,023	11.0
Plants	978	10.5
Metals and plating	726	8.0
Dyes, including fur dyes	492	5.5
Chromic acid and chromates	478	5.5
Acids	312	3.5
Rubber and its compounds	253	2.7
Resins	164	1.8
Physical agents	143	1.5
Biologic agents	112	1.2

The apparently harmless clothing and textile industries come next, and it will be noted that they are just ahead of the hazardous chemical industry. This is so because the hazards in the chemical industry are recognized and proper safety precautions are taken and because the number of workers in the chemical industry in the states from which these statistics were gathered is probably not as large as the number in the clothing and textile industries. There are far fewer safety precautions, such as totally enclosed processes, protective clothing, compulsory shower baths and exhaust ventilation in the seemingly less hazardous industries than there are in the industries having well known hazards. Hence the skin of food handlers and domestic servants is exposed to the action of strong soaps and other cleaning solutions and the number of cases of dermatosis among them is second only to that among the workers in the metal industries.

The ten leading chemical causes of occupational dermatoses as shown in table 4 are (1) petroleum oils and greases, 14 per cent; (2) alkalis, including cement and concrete, 10 per cent; (3) solvents, 10 per cent; (4) chromic acid and salts, 7 per cent; (5) metals, including metal plating, 6 per cent; (6) dyes, 5 per cent; (7) plants, 5 per cent; (8) rubber and its compounds, 3 per cent; (9) paints and varnishes, 3 per cent; (10) synthetic resins, 2.5 per cent.

Table 5 gives a combined analysis of tables 3 and 4 as to cause. In this table the figures for alkalis should be combined with those for building cement and the figures for solvents with those for paints, enamels and varnishes. Arranged in this order the list reads as in table 6.

SUMMARY

It is difficult to correlate accurately the records gathered by many observers from various localities and industries regarding the occurrence of occupational dermatoses. Nevertheless, these records combined with the inspections, studies and experiences of the United States Public Health Service in many of the leading American industries lead to the conclusion that the annual incidence of occupational dermatoses in the United States is at least 1 per cent for all industrial workers; that 30 per cent of the cases occur in the metal

industries; that the domestic and food industries come second and third, respectively, in furnishing cases of occupational dermatosis; and that alkalis, petroleum products, solvents, plants metals and metal plating; acids, including chromic acid, dyes, rubber compounds and resins are the leading chemical causes.

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INDUSTRIAL DERMATITIS

DEFINITIONS AND CRITERIA FOR DIAGNOSIS

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This communication forms only a small part of the present symposium on occupational dermatoses. We therefore assume that our exposition need not (and indeed cannot) be considered alone but is to be regarded as forming an integral part of the entire presentation.

For this reason we may here deal with specific isolated points and enter directly into their discussion without preamble. However, the first portion of this paper attempts to fulfill a function which is so fundamental and so necessary that it might well have been considered as an essential preface to the entire program.

Definitions, difficult and dry and disagreeable as they may be, are nevertheless an unavoidable necessity for intelligent discussion; and on close analysis one finds that many so-called scientific discussions are, unfortunately, based more on arguments as to definitions than on deliberations as to facts.

DEFINITIONS

We believe that no one will quarrel with the following definitions of dermatosis and dermatitis:

A dermatosis is a disease, or pathologic condition, of the skin.

A dermatitis is an inflammatory disease or condition of the skin (i. e. a subcategory of dermatosis).

If we now define the words occupational and industrial and qualify these two definitions with them, we shall arrive at logical composite definitions of occupational dermatosis and dermatitis and of industrial dermatosis and dermatitis.

The Oxford dictionary¹ describes an occupational disease as "a disease incidental to one's occupation," and occupation is described as "an employment, business, calling." Moreover, it defines industry as "systematic work or labor, habitual employment, now especially in the productive arts or manufactures."

It will thus be seen that an occupational dermatitis may be defined as "an inflammatory condition of the skin incidental to one's occupation" (e. g. "housewife's eczema," dermatitis from golf clubs or plants in the golf instructor and dermatitis from the top of a desk or from dictaphone cylinders in the proprietor of a real estate business).

These definitions make clear that not all occupational dermatitis need also be industrial dermatitis. Industrial dermatitis must be regarded as a subcategory of occupational dermatitis; it is "an inflammatory condi-

tion of the skin incidental to systematic work or labor or habitual employment, especially in the productive arts or manufactures."

All this appears to be so simple and so forthright, so utterly beyond controversy, that it seems incredible that there should be difficulties in reaching a decision as to whether a given condition is or is not an inflammatory condition of the skin incidental to the patient's industrial employment.

It must be recognized, however, that not only non-dermatologists and physicians outside of industry but even dermatologists and specialists in industrial medicine, unfortunately, will often be unable to decide whether certain conditions are of an industrial nature.

As we see it, three among the principal reasons for these almost constant difficulties are proper subjects for discussion here.

I. THE TENDENCY TO CONFUSE PURELY MEDICAL CONSIDERATIONS WITH LEGAL INTERPRETATIONS

A first reason for the difficulty of medical decision seems to us to be based on the fact that physicians have often allowed themselves to become involved in questions of jurisprudence rather than of medicine. In the realms of language, of logic, of justice or of medicine an industrial dermatitis is any inflammatory disease of the skin for which any effect of industrial occupation can be proved to be a principal or major, causal or contributory, factor. In the eyes of the law, however, and for undeniably practical reasons, in many cases such a condition cannot today be compensated and therefore cannot be legally defined as industrial in nature. In other words, the question of the industrial nature of a disease is decided from the medical point of view by considerations which remain unchanged. The medical criteria remain the same regardless of laws, political boundaries, sociologic conditions, governments, policies, economic systems or times, whereas the actual legal definition as to what constitutes an industrial disease and particularly as to what is to be considered a compensable disease, the legal point of view in short; must vary according to all these factors. Thus it often suffices to cross a river or to step across a state line to find a complete change in the legal criteria as to the compensability in a given case. This condition of affairs has necessarily proved to be confusing, and the medical testimony has too often tried to go beyond the purely medical considerations and to answer the questions as to the legal status and as to the compensability in a given case. We believe therefore that physicians should confine themselves to the medical decision and always endeavor to ascertain as correctly and to state as clearly as possible the degree of probability with which the industrial exposure was or was not a major factor in a given case. We believe that the physician should not allow himself to be disturbed or distracted by the consequent interpretations or questions of legal status. The physician's answer can be clear: (1) "My findings lead me to conclude that the presenting dermatitis is in all probability to a major degree dependent on the patient's industrial exposures"; (2) "my findings lead me to conclude that the presenting dermatitis is not in all probability to a major degree dependent on the patient's industrial exposures," or (3) "the medical findings are such that I cannot decide whether the presenting dermatitis is or is not to a major degree dependent on the industrial exposures." These must be the three possible final conclusions permitted by the purely medical considerations, beyond which the physician cannot, and indeed should not, venture.

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1. The Shorter Oxford English Dictionary, London, Oxford University Press, 1936.

However, even when the physician in this manner confines himself most strictly to medical decisions, why is it that he must so often say "I cannot decide whether the industrial exposure was or was not a major factor in this case of dermatitis"? While this admittedly unsatisfactory answer must frequently be given regarding other conditions as well, it is the only honest answer in a greater number of cases of "eczema" than of any other type of compensation cases. The reason lies in the inherent and peculiar difficulties which eczematous dermatitides present to an infinitely greater or more apparent degree than does any other category of industrial diseases.

II. UNCHARACTERISTIC APPEARANCE AND COURSE OF ECZEMATOUS DERMATITIS

The second characteristic difficulty which so frequently renders the decision as to the causal role of industrial exposures particularly and peculiarly complicated in cases of industrial dermatitis is the fact that frequently the appearance and course of eczematous dermatitis is not characteristic, indicative or diagnostic of the actual causal agent.

The clinical manifestations of infection with a micro-organism (e. g. tuberculosis, tinea, actinomycosis and anthrax) usually permit a conclusion as to the causal agent and often as to the time of the occurrence of exposure. Poisoning due to arsenic, lead, carbon tetrachloride, benzene or other volatile solvents regularly produces signs and symptoms from which the physician can determine the character of the noxa and thus often the approximate time at which the exposure occurred. The manifestations of such diseases as silicosis, of x-ray or tar cancer, of damage due to radium, as well as of a host of other conditions, often point directly and unmistakably to causal agents and to the place and time of the harmful encounter. For these reasons the proof of industrial causation is often as

TABLE 1.—Medical Definition and the Distinction Between Medical and Legal Criteria

DEFINITION
An industrial dermatitis is any inflammatory disease of the skin for which industrial exposure can be shown to be a major causal, contributory or eliciting factor. (Industrial dermatitis is a subcategory of occupational dermatitis, for occupational dermatitis includes not only industrial dermatitis but also all other dermatitides attributable to any occupational pursuit.)
PROOF
For the physician the proof of the industrial nature of a dermatitis must depend entirely on medical and not on legal considerations. From the medical point of view there cannot be proof absolute of the wholly industrial nature of the disease in a given case, but there are nevertheless certain medical criteria which indicate with a high degree of probability whether or not in a certain case the dermatitis can be considered in major part attributable to the industrial occupation of the affected person.

clear in the case of such conditions as in the case of industrial accidents and injuries.

With eczematous dermatitis, on the other hand, the situation is different. This difference must be recognized as being of the utmost practical significance when one realizes that industrial eczematous dermatitis seems to be by far the most common of all industrial diseases; that it is apparently so common that the number of cases of industrial dermatitis probably exceeds the number of cases of all other industrial diseases combined. Industrial eczematous dermatitis, like all other eczematous dermatitis and in contrast to those diseases in which the clinical picture often indicates the cause, has

a clinical picture and course which do not as a rule permit a conclusion as to causal agents. For, while it is true that in many typical cases an expert can recognize, for example, whether a dermatitis is due to a plant such as poison ivy or to a dye such as paraphenylenediamine, it is equally true that dermatitides from plants, dyes, solution of formaldehyde, soap, gloves, a cosmetic preparation, a medicament,

TABLE 2.—Medical Criteria for Establishing Proof of the Probable Industrial Nature of a Given Dermatitis

Criteria of the First Order
1. <i>Inception:</i> The dermatitis appears at any time during a period of industrial exposure or even after a lapse of a reasonable incubation period following the cessation of the industrial exposure (usually a maximum of from two to three weeks).
2. <i>Amelioration:</i> The dermatitis regularly disappears or is repeatedly improved within a reasonable period (days, weeks or even months) after cessation of the causal industrial exposure. (While this is usually the case, retention of causal agents, complications or ensuing polyvalent sensitization may prolong the course even for several years after the last industrial exposure.)
3. <i>Recurrences and Exacerbations:</i> The dermatitis shows a tendency repeatedly to recur or to exacerbate when the worker returns to the identical industrial exposure after a certain period of absence (provided there has been no change in working conditions or in the patient's manner of working or in his susceptibility).

fungi or even friction and injuries may look and act exactly alike. They may then be clinically indistinguishable from one another even by the most experienced physician and may sometimes remain indistinguishable even after considerable investigation. The physician is thus often unable to decide whether or not in a given case the dermatitis is actually due to the industry or is due to some other home or non-industrial extrinsic or intrinsic factor. For these reasons, as well as for other reasons which will soon be discussed, special forms of investigation and special criteria are often necessary in attempting to reach an opinion as to the industrial or nonindustrial causation in a given case of dermatitis. We present these criteria in tabular form, the tables representing only a slight modification of similar tables previously published elsewhere.²

It is obvious that with industrial dermatitides the situations which arise are often complex and extremely variable from case to case. For this reason a brief schematic presentation, such as these tables represent, cannot be expected to cover all contingencies or to fit all circumstances. These tables are intended only as a rough, rule of thumb guide, as a framework on which to build the actual structure of investigation and decisions applicable in the given case. It is to be hoped that, in spite of their many inevitable inadequacies, these tables will be of some assistance to physicians who are called on to make difficult decisions as to the industrial nature of certain dermatitides.

III. SYNERGISTIC REACTIONS

Another difficulty encountered in determining whether or not a dermatitis is due to an industrial exposure lies in the fact that many eruptions are due not to a single simple cause but to an interaction of many causes and to a complex effect attributable to the cooperation of many factors. This may be termed the synergistic (synergic) action of various agents or the composite etiology of eczematous dermatitis.

2. Sulzberger, Marion B.: Determining the Industrial Nature of a Dermatitis, New York State J. Med. 26: 1307 (Sept. 15) 1936.

According to present concepts, few if any diseases are due to one simple, uncomplicated effect or to a single causal agent. Even when the part of a single causal agent seems unequivocally dominant and is clearly discernible, it is necessary to recognize and to evaluate the role of preceding and/or concomitant contributory and predisposing factors. The complex interaction of various forces in the production of disease is perhaps most clearly apparent in the genesis of certain diseases of the skin, and it is probable that, for this reason, dermatologists were among the first to recognize and to describe and study the role of synergy in the pathogenesis of disease. Cases of eczematous dermatitis offer many striking examples of the importance of complex and synergic effects, and in the case of eczematous industrial dermatitis the complexity of etiologic factors presents constant difficulties to physicians striving to reach categorical decisions as to causation. The actual mechanisms of these synergic etiologic forces are just beginning to become amenable to scientific and laboratory study.

Among the long-recognized examples of synergy, we may mention first the fact that one allergen may sensitize the skin and that this first sensitization may be observed, by some unknown mechanism, to pave the

manifestations. Among other examples of this type we may mention tubercloid leprosy and tubercloid syphilis, in which, as Jadassohn³ pointed out, the hypersensitivity of the cutaneous lesions is present but is directed not only to leprolin and to luetin, respectively, but often also to tuberculin.

TABLE 4.—Some Common Causes of Erroneous Conclusions That a Dermatitis Is of Industrial Causation

The dermatitis is erroneously considered to be industrial because:

A. It is a dermatitis affecting a worker in an industry notorious for the occurrence of that type of dermatitis. (For example, dermatitis venenata may be due in the specific case to nonindustrial exposures; home exposures to dyes, cosmetics, toilet articles, insecticides, clothing, paint, varnishes or plants or exposures to substances encountered in hobbies or avocations, such as photography, painting or sports.)

B. It is accompanied by a reaction to a patch test with a substance or substances encountered in the industry. (Such a reaction to a patch test cannot be considered conclusive, for [1] it may be due to the application of a primary irritant or of a primary irritant concentration and [2] since the test never accurately reproduces the conditions of actual industrial exposure, a reaction may mean simply sensitivity of the skin to a certain substance when applied in a certain concentration and manner at a certain time to a certain site, while the same substance may be incapable of causing dermatitis under the actual conditions of industrial exposure.)

The common observations that quiescent sites of patch tests or quiescent sites of intracutaneous or other forms of skin tests may "flare up" when the same, or even when entirely unrelated, allergens are administered at a distant site are clear illustrations of synergy. In this category of phenomena we may also place many other well known dermatologic manifestations, such as those in certain fixed drug eruptions. One sometimes finds that areas first sensitized and at first reacting only on exposure to one specific drug, such as phenolphthalein, subsequently "flare up" after administration of a nonrelated drug, such as arsphenamine, a preparation of gold or a barbiturate. Moreover, the sensitivity to iodine often found with dermatitis herpetiformis and with acne vulgaris or the sensitivity to agar found with tertiary syphilis⁴ necessitates the hypothesis that the disease agent has in some way produced a sensitivity—in the widest sense of the word—to unrelated substances (allergens?).

There are also the many instances in which it can be shown that infectious processes or sensitization to the products of micro-organisms lead to susceptibility to sensitization to nonliving allergens. The studies of Stokes and his associates⁵ of the effect of seborrhea of tinea and of other foci of infection in increasing the susceptibility to arsphenamine dermatitis, the cases in which a dermatitis clears up when the tonsils, gall-bladder or other foci are eliminated and the case reported by Jadassohn⁶ of a house painter who became susceptible to industrial exposures only after severe nephritis are but a few of the instances which could

TABLE 3.—Medical Criteria for Establishing Proof of the Probable Industrial Nature of a Given Dermatitis

Criteria of the Second Order (Adjutant Criteria)

1. The dermatitis appears first in, and is usually confined to, the areas of maximum exposure (in a small percentage of cases it spreads to, or may begin in, apparently unexposed areas or even becomes generalized).
2. The character and localization of the dermatitis correspond to the character and localization of dermatitis known in other cases to have been caused by exposure to the same or similar industrial hazards. (While many different substances and procedures can produce similar or identical eruptions, there are certain classes of substances and of procedures which regularly produce fairly characteristic lesions.)
3. The application of the presumptive causal agents to an unaffected site close to the site of the dermatitis produces a reaction, provided this application is made either during the active phase or after the proper interval following the cessation of the dermatitis.
4. The cutaneous tests produce reactions of the same fundamental nature as the dermatosis under investigation.
5. Other workers similarly occupied are or have been similarly affected.
6. The dermatitis appears soon (days or weeks) after the patient begins work involving new potential hazards.
7. The dermatitis is proved to be of possible occupational nature; that is, it is shown to be of the type which may result from the industrial exposure sustained. In this connection it must be determined that the dermatitis under consideration is not a nonindustrial eruption of such dermatoses as seborrheic dermatitis, psoriasis (including pustular psoriasis), parapsoriasis, lichen planus, dermatitis herpetiformis, multiform erythema, certain types of nonindustrial fungoid and other infectious processes, nonindustrial impetigo and other pyodermas, acrodermatitis continua, nonoccupational drug eruptions, herpetic eruptions, nevoid and other anomalies of the skin, nonindustrial dermatitis exfoliativa, circumscribed neurodermatitis, atopic dermatitis and, particularly, nonindustrial contact-type dermatitis. (It must, however, be borne in mind that the presence of a nonindustrial dermatosis by no means excludes the possible coexistence of an industrial dermatitis. Moreover, the existence of a nonindustrial dermatosis may predispose to industrial dermatitis; and, on the other hand, industrial exposures may elicit attacks, prolong the course or produce exacerbations of such nonindustrial dermatoses.)

way or bring in its train a subsequent sensitization to a second or third or greater number of perhaps entirely unrelated allergens. Cases which illustrate this effect are those in which sensitization to arsphenamine is followed by sensitization to bismuth or to mercury, so that subsequent to arsphenamine dermatitis the previously well tolerated preparation of bismuth or mercury cannot be administered without causing cutaneous

3. Jadassohn, Josef: Bemerkungen zur Sensibilisierung und Desensibilisierung bei den Ekzemen, *Klin. Wchnschr.* 2: 1680 (Sept. 3), 1934 (Sept. 17) 1923.

4. Stokes, John H.: A Luetin Reaction in Syphilis Produced by Agar: I. J. Cutan. Dis. 32: 560, 1914; 11. J. A. M. A. 68: 1092 (April 14) 1917. Clausz, Max: Diagnostische Versuche mit Luetin-Nocuti München, med. Wchnschr. 61: 1933, 1914. Sherrick, J. S.: The Effect of Potassium Iodide on the Luetin Reaction, J. A. M. A. 65: 404 (July 31) 1915. Cole, H. N., and Paryzek, H. V.: The Provocation of the Luetin Test in Nonsyphilitic Patients, J. A. M. A. 68: 1089 (April 14) 1917. Barker, Leslie P.: Value of Organic Luetin in Diagnosis and Treatment of Syphilis, Arch. Dermat. & Syph. 3: 676 (Nov.) 1934.

5. Stokes, John H., and Cathcart, E. P.: Contributory Factors in Post-arsphenamine Dermatitis with Special Reference to the Influence of Focal and Intercurrent Infection, Arch. Dermat. & Syph. 7: 14 (Jan.) 1923. Stokes, John H., and Kulchar, G. V.: Infection-Allergic Complex in Arsphenamine Dermatitis Reactions, with Special Reference to Dermatomyositis, Brit. J. Dermat. 46: 134 (March) 1934.

6. Jadassohn, Josef: Die Toxicodermien, *Deutsche Klin.* 10: 117, 1905.

be mentioned here. Here also belong the almost innumerable cases of dermatophytosis leading to subsequent sensitizations and to subsequent dermatitis from simple chemicals or from other external contact allergens, as so well described by White and Taub,⁷ Osborne and Putnam⁸ and others.

In addition it is all too common to see the synergic relationship between allergens or noninfectious factors and infectious organisms illustrated in the reverse sequence. Recurrent herpes simplex is a common but excellent and striking example. It can be shown that chocolate, nuts, shellfish, drugs, sunlight or some other factor or factors, including psychoneurogenous effects, will in some cases allow or impel the dormant but ever present virus suddenly to produce characteristic manifestations, which may be reproduced by the same factors and often in the same sites with the regularity of a laboratory experiment. Mention may be made also of the clinically common and important appearance of exacerbations of dermatophytosis (sensitization to fungous products) subsequent to sensitization to simple eczematogenous allergens.

In short, among the dermatologic illustrations of complex etiologic and synergic effects there are an almost endless number and a practically infinite variety of well known and universally accredited phenomena which prove the thesis that the cause of most diseases of the skin is made up of not one but many factors. Many of these phenomena may be classified according to nomenclature as manifestations of either specific or nonspecific polyvalent sensitizations (Jadassohn, Bloch) and many can be placed in the category of either metal allergy or parallergy (Urbach) or of biotropism of Milian.

In addition to this summation or potentiation of allergenic effects, one must bear in mind the effects of constitutional, acquired or hereditary, permanent or transitory, local or systemic, predisposing causes. These may be simple, such as too dry and too easily fissured skin and ichthyosis, too oily skin, hyperhidrosis, or lack of adequate protective sebum, protective pigment or elastic fibers. Or they may be more complex, such as atopy, hepatic insufficiency, diabetes or circulatory disturbances. The predispositional factors may be toxic or metabolic (e. g. absorption of bacterial toxins or products from the gastrointestinal tract and porphyrin), or they may be due to products of faulty digestion or to a deficiency, such as an insufficient vitamin supply, inadequate vitamin retention or faulty vitamin utilization. To all these physicochemical factors we must not fail to add the imperfectly understood, highly complicated and all too frequently invoked, but nevertheless sometimes undeniably present and occasionally quite apparently potent, influences of psychic and emotional states⁹ and the synergy of these states with any or all of the mentioned factors.

Our exposition of this phase of the subject is deliberately rudimentary, and we have made it a point to mention only a few of those synergistic phenomena which would immediately present themselves to the mind of the dermatologist. Not one of our examples is new, and almost all the mentioned categories, as

well as many others, have been discussed and studied by dermatologists for over forty years. Persons who are interested in further details and in a masterly exposition of many of the early phases of this subject are advised to read the pertinent original contributions of Josef Jadassohn.¹⁰

In spite of the innumerable and long-established clinical observations and facts in this field, the exact mechanism of etiologic synergy and of complex additions and multiplications of effects has scarcely begun to be understood. It is therefore most welcome that laboratory workers are beginning to become cognizant of these matters and that it may be hoped that experimental studies will soon bring some greater measure of understanding. Examples of the increased volume of recent laboratory work which touches on these

TABLE 5.—Some Common Causes of Erroneous Conclusions That a Dermatitis Is Not of Industrial Causation

The dermatitis is erroneously considered to be nonindustrial because:

A. It is accompanied by the finding of fungi or other micro-organisms in the lesions or in a distant focus. (Fungi, pathogenic and nonpathogenic, and certain other micro-organisms, e. g., staphylococci, streptococci, yeasts and molds, are almost universally found on the skin of adults in the United States. Their demonstration does not therefore constitute proof that a dermatosis is of nonoccupational nature.)

B. It is accompanied by a cutaneous reaction to tests with extracts of fungi or of certain other micro-organisms. (Such reactions are too common to be of weight in ruling out the industrial nature in a given case; they merely show that the patient has had a prior sensitizing exposure to the same or to an immunologically related micro-organism; they are comparable to reactions to tuberculin in the general population.)

C. The reactions to patch tests with the substances of the industrial exposure are negative. (Such negative results of patch tests cannot be considered conclusive. They may be due to: [1] Local differences in sensitivity. The area tested may not be hypersensitive, while other areas, particularly the areas involved, may be hypersensitive. [2] Chronologic differences in sensitivity. A person's skin, sensitive at the time of industrial contact, may be nonsensitive to the actual causal substances at the time of testing. [3] The fact that the actual causal substance or substances or the causal combination or causal intermediates may not have been applied. [4] The fact that the concentration employed may have been too weak, that the test application may have been otherwise inadequate or that the vehicle employed may have been incorrect or may have prevented penetration or exerted some protective or neutralizing effect; e. g. water instead of sweat, fat or oil instead of an aqueous vehicle or vice versa, acid instead of alkali or vice versa. [5] The fact that the test never accurately reproduces the actual conditions of industrial exposure. Repeated contact, friction, maceration, heat, cold, sweat or other industrial agents or processes may be necessary additional factors enabling the substance, giving negative results in the test, to cause dermatitis under conditions of industrial exposure.)

problems are the studies of Luithlen, Hahn, Mayer and Sulzberger,¹¹ Sulzberger and Oser¹² and Cormia¹³ on the effects of diets and environments in the inhibition and augmentation of susceptibility to sensitization; Pillsbury and Sternberg¹⁴ on the sugar content and irritability of the skin; Dienes and Schoenheit¹⁵ on the synergism of tuberculin or tuberculosis and simpler

7. White, Cleveland, and Taub, S. J.: Sensitization Dermatoses of Nonlupous Nature Following Superficial Fungous Infections ("Ringworm") of Extremities, *J. A. M. A.* **98**: 524 (Feb. 13) 1932.

8. Osborne, Earl, and Putnam, E. D.: Industrial Dermatoses with Special Reference to Allergy and Mycotic Dermatitis, *J. A. M. A.* **99**: 972 (Sept. 17) 1932.

9. Stokes, John S., and Pillsbury, Donald: The Effect on the Skin of Emotional and Nervous States, *Arch. Dermat. & Syph.* **22**: 962 (Dec. 30) 1930.

10. Jadassohn, Josef: Zur Kenntnis der *Medicine* . . . sen, Verhändl. d. deutsch. dermat. Gesellsch. . . . and Praktisches zur Ekzemlehre, *Ztschr. f. ärztl.* . . . 1) 1929; A Contribution to the Study of Dermatoses Produced by Drugs, Selected Essays and Monographs **170**: 207, 1900; Hematogenous Infectious Diseases of the Skin, *Arch. Dermat. & Syph.* **21**: 526 (April) 1930; footnotes 3 and 6.

11. Mayer, R. L., and Sulzberger, Marion B.: Zur Frage der jahreszeitlichen Schwankungen der Krankheiten: Der Einfluss der Kost auf experimentelle Sensibilisierungen, *Arch. f. Dermat. u. Syph.* **163**: 245, 1931.

12. Sulzberger, Marion B., and Oser, Bernard L.: Influence of Ascorbic Acid of Diet on Sensitization of Guinea Pigs to Neocarphenamine, *Proc. Soc. Exper. Biol. & Med.* **22**: 716 (Feb.) 1935.

13. Cormia, Frank E.: Experimental Arsenphenamine Sensitization, *J. Invest. Dermat.* **1**: 199, 1938.

14. Pillsbury, Donald M., and Sternberg, T. H.: Relation of Diet to Cutaneous Infection, *Arch. Dermat. & Syph.* **35**: 893 (May) 1937.

15. Dienes, L., and Schoenheit, E. W.: Certain Characteristics of the Infectious Processes in Connection with the Influence Exerted on the Immunity Response, *J. Immunol.* **19**: 41 (July) 1930.

protein allergens; Burky¹⁶ in his important work on the synergism of bacterial toxins and sensitization to body-own substances (lens, muscle); Swift and Schultz¹⁷ on the same subject; Schwartzman and his co-workers¹⁸ on the synergism of certain bacterial endotoxins as local factors preparing the skin to respond with hemorrhagic lesions on hematogenous exposure to a variety of eliciting agents which when acting alone are incapable of producing this effect; Schwentker and Rivers¹⁹ on the synergism of virus and cerebral and neural lipid extracts in enhancing the formation of organ-specific antibrain (antimyelin) antibodies, and Rous and Beard²⁰ and Rous and Kidd²¹ on the synergism of Shope papilloma virus, of tar and of scarlet red in the more rapid production of carcinomatous changes in the rabbit's skin. Extensive experimental studies of this type justify the hope that greater clarity will soon be forthcoming and that the clinician may some day be helped materially in his endeavor to determine the relative significance of various factors in the production of a single disease in each particular case.

In the field of industrial dermatology today the complications arising from factors such as those described and the difficulties of determining the exact proportion of causal effect attributable to any single factor or group of factors still represent the greatest, often insurmountable, handicaps in the attempt to decide as to the industrial nature of a dermatitis.

We shall cite only two examples here, both taken from actual experience and both surely duplicated ad infinitum in the practice of all industrial dermatologists.

The first illustrates the fact that an industrial exposure may lead to or predispose toward subsequent irritation of the skin from nonindustrial causes:

CASE 1.—A worker previously without dermatosis was exposed to solution of formaldehyde. Sensitization developed. A proved formaldehyde dermatitis appeared on the hands, arms and face. Subsequent to this, for a period of years and without any apparent further exposure to formaldehyde, a chronic recurrent eczematous dermatitis ensued. Myceliums of fungi were found in the new eczematous eruption on the feet and toes.

In a case such as this what proportion of blame shall attach to the industrial sensitization?

The second case illustrates a second large class of common complications, namely those based on the fact that nonindustrial factors may lead to or predispose toward subsequent irritation of the skin from industrial exposure:

CASE 2.—An employee who as far as could be ascertained had never before suffered from a dermatosis took a therapeutic dose of a proprietary preparation containing quinine. From this time on she found it impossible to continue her work as a beauty shop operator because of chronic recurrent dermatitis of the hands and face. Patch tests proved her to be strongly

hypersensitive to quinine. When she stayed away from her work the dermatitis disappeared, only to recur on each return to the previous occupation.

In this case how shall the physician answer the question as to whether or not the occupational exposure represents a major factor?

Innumerable multiplications and modifications of these two types of sequence are possible. There are the cases in which fungous infections lead to subsequent industrial dermatitis, and vice versa. There are the cases in which nonindustrial exposures (sunburn, trauma, sensitizations) lead to specific monovalent or polyvalent industrial sensitivity or simply to nonspecific polyvalent irritability leading, in turn, to industrial dermatitis. There are the countless cases in which not only do one industrial effect and one extra-industrial effect act as synergists but many synergistic forces are at work. These forces may be the result chiefly of industrial exposures, or they may be distributed in any proportion between nonindustrial and industrial causes. A most common combination of multiple causation is seen, for example, in the case of dishwashers, soda fountain clerks and others engaged in occupations entailing prolonged exposure to water, soap and other cleansers. Maceration, plus caustic action, plus the extraction of protective sebum, plus infection of the skin with micro-organisms such as cocci, yeasts and other fungi, plus friction, plus allergens and irritants (e. g. from nickel plate, from vegetables, from fruit juices) plus a definite degree of extra-industrial local or constitutional predisposition form the most frequent causal combinations.

CONCLUSION

Although we feel that we have outlined a sketch rather than painted a picture, we believe that our presentation may suffice to convince that our subject is complicated and full of innumerable difficulties and pitfalls. Because of the complexity of the subject we have employed the accompanying tables, which at first glance undoubtedly appear to be unnecessarily complicated and lengthy. Because of this complexity, moreover, we freely admit a conviction that such tables, no matter how detailed, will all too frequently prove to be woefully inadequate.

We should like to emphasize the following points:

1. For the physician the question of deciding as to the industrial nature of the dermatitis in a given case should remain a purely medical one.

2. The nondiagnostic appearance of many eruptions of eczematous dermatitis and the synergistic action of complex factors in their causation, as well as other special complicating factors, often make it impossible to decide what portion of causal blame shall attach to industrial exposures.

3. The complexity and intricacies of these problems are such that (a) they urgently require further clinical and, especially, further laboratory study; (b) only impartial experts can be expected to hold valued opinions as to moot cases, and (c) in many cases even the longest and most painstaking study, even the most logical, complete and exact tables of criteria and even the greatest experience and clinical acumen leave the honest physician no alternative but to answer "In this case I do not know and cannot determine whether or not the industrial exposure was the major factor."

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THE PRACTICAL ASPECT OF THE
PREVENTION OF INDUSTRIAL
DERMATOSES

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It is generally admitted that industrial dermatoses are responsible for from 40 to 60 per cent of all claims for the payment of compensation in the United States.¹ This percentage varies depending on the type of industry chiefly present in the individual states. The more highly industrialized the state or country, the higher is the percentage of claims as a result of industrial dermatoses. It is obvious that effort directed toward the reduction of the incidence of industrial dermatoses would materially reduce both the direct and the indirect cost of these conditions to the employer, the employee and the public. It is our belief that the cost of industrial dermatoses could be reduced at least 50 per cent if all the scientific facts now available were put to use. It is our purpose in this paper to summarize these facts and to discuss their application.

It is impossible to discuss in one paper the prevention of all cutaneous disease arising as a result of industrial injury. Therefore we will discuss only the more common and important industrial dermatoses, especially industrial dermatitis, which represents by far the greatest problem in industrial cutaneous medicine.

INDUSTRIAL DERMATITIS

Industrial dermatitis is the most common cutaneous hazard in American industry. It outranks all other industrial conditions of the skin from the standpoint of time lost from work, money spent in compensation, suffering and unemployment. The term industrial dermatitis includes (a) inflammation of the skin due to primary irritants, such as strong acids, alkalis, metallic salts, soaps, cleansers and physical agents, in non-allergic persons and (b) sensitization dermatitis, in which a specific cutaneous sensitivity is the underlying factor. In the case of dermatitis due to primary irritants, the first contact with the irritant in sufficient concentration, or prolonged contact with weaker dilutions, is capable of setting up the dermatitis. In the case of dermatitis due to specific cutaneous sensitivity, a well defined period of sensitization is necessary, during which period the substance is handled with impunity unless in sufficient concentration to produce primary irritation. After sensitization develops, the subject reacts to a dilution of the allergen far greater than that necessary to produce dermatitis in a normal or unsensitized person. Many substances used in industry are not only primary irritants and thus capable of producing dermatitis in normal persons but also of producing dermatitis in normal persons but also of producing dermatitis in normal persons but also of producing a characteristic sensitization dermatitis. This phenomenon is particularly prevalent in the case of persons who come in contact with turpentine, gasoline, chromium, soaps, alkalis, certain acids, chemical salts

or formaldehyde. It is of the utmost importance in the prevention of industrial dermatitis to differentiate at once between an inflammatory reaction due to primary irritation and an inflammatory reaction due to the development of true hypersensitivity. According to our experience, persons who have suffered from a primary chemical irritation are much more liable to have a true sensitization dermatitis with further repeated contacts with the chemical.

DERMATITIS FROM PRIMARY IRRITANTS WITH
NO ALLERGIC FACTOR

Many chemicals and industrial compounds are capable of producing dermatitis in workers who have no specific cutaneous sensitivity. Among these substances are acids, alkalis, hypertonic solutions, soaps, gases, vapors, fat solvents, cement, plaster, lye, metallic oxide and hot water. These agents may exert their action on the skin, according to White,² by (1) dissolving the horny layer, (2) dissolving the protective natural grease on the skin, (3) protein precipitation, (4) desiccation, (5) dissociation or hydrolysis in water to form irritating compounds from nonirritating substances, (6) oxidation or (7) reduction. The type and degree of reaction depends on the character of the substance, the concentration and the degree of exposure to the irritant. Persons do not all react in the same manner to these irritants. Anatomic and physiologic differences in workers' skins play an important part. Persons with thin blond skin or with dry, ichthyotic skin whether it is the result of congenital ichthyosis, old age or environmental conditions are more readily affected. Primary irritative dermatitis is more prevalent during the winter months, when the sebaceous and sweat glands are less active and the humidity is low in homes and workshops.

PREVENTION OF NONALLERGIC IRRITATIVE
DERMATITIS

Although the incidence of nonallergic irritative dermatitis in American industry is high,³ there is little excuse for its development, since for its production relatively high concentrations or long periods of exposure are required. Mechanical means of protection and education of the worker will usually suffice to prevent this type of dermatitis. Protection includes the use of acid-resisting and alkali-resisting gloves, aprons and shields. Impervious pastes are sometimes of great value. Adequate facilities for cleansing the exposed parts should be readily available.

Irritating fumes and dust should be removed at their source by properly installed suction hoods and adequate ventilation. This type of apparatus has proved its efficacy in numerous lines of industry.⁴ Obviously such removal calls for close teamwork between the industrial engineer and the industrial dermatologist.

In many instances a simple irritative dermatitis is caused by agents used to cleanse the skin after work rather than by substances handled in the course of the daily job. Fat solvents, such as gasoline and turpentine, and strong alkalis, including soaps used to cleanse the skin after work, have frequently been found to be the cause of an irritative type of dermatitis.

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As stated previously, a simple irritative nonallergic dermatitis is in most instances preventable. It may lead to a more complex, disabling sensitization dermatitis. This is well illustrated by the following case:

A valued workman who had been with a high class wallpaper concern for thirty years had a turpentine burn on his fingers, which, although he was warned, recurred over a period of five or six years. Contrary to instructions, he continued to come in contact with full strength turpentine from time to time. Suddenly, for no apparent reason, he had extensive dermatitis on the hands, forearms, face and neck. He reacted violently to a 1 to 500 dilution of turpentine in liquid petrolatum. He had generalized exfoliative dermatitis after further exposure and has since been unable to enter a room in which turpentine is present in the air. In addition to being disabled for nearly two years, he has had to seek other work at a fraction of his former salary. Adequate prevention of contacts in the first place, with the prevention of irritative dermatitis, would in all probability have prevented the subsequent sequence of events.

Not only does primary irritative dermatitis lead to sensitization dermatitis to the same substance but, as is well known and recognized by dermatologists, any area of inflamed skin easily acquires further sensitivities to contacting allergens. We believe that simple irritative dermatitis should never be passed over lightly but that adequate means of protection should be provided and the employee warned regarding further contact with the offending substance.

SENSITIZATION DERMATITIS

Experience has shown that almost any chemical compound will produce sensitization dermatitis if the duration of exposure and concentration are sufficient. With the rapid advance of chemical research and the development of new chemical compounds, the number of these substances is daily getting larger and larger. Not only are workmen exposed to numerous eczematizing agents at work but also they are exposed in their homes and during their periods of recreation to a whole gamut of potential cutaneous allergens.

Many industries present greater hazards than others. Workers with dyes,⁵ formaldehyde,⁶ lacquers,⁷ turpentine,⁸ chromium,⁹ nickel,¹⁰ resins¹¹ and munitions¹² are more apt to be sensitized than workers in other industries.

PREVENTION OF SENSITIZATION DERMATITIS

The prevention and control of sensitization dermatitis is the greatest problem confronting the industrial dermatologist. The development of severe sensitization dermatitis may mean weeks or months of disability and, too often, a change in occupation. Frequently, at least in cases of severe involvement, multiple sensitization occurs. Instead of reacting to one offending allergen, the workman then reacts to many substances, not only at work but at home. The problem of preventing sensitization dermatitis primarily resolves itself into four phases: (1) the proper selection of workers, (2) the elimination of unnecessary hazards, (3) the prevention of exposure to sensitizing substances and (4) the early

recognition of sensitization dermatitis and the prevention of further contacts with substances having a high sensitization index.

Before these different phases are discussed in detail, it is necessary to summarize some of the pertinent facts regarding sensitization to chemical compounds. It is well known that certain persons are more easily sensitized than others. Some persons become sensitized with the first contact and others only after weeks, months or years of repeated exposures. It has been repeatedly demonstrated that all persons become sensitized more readily with strong concentrations than with weak. The greater the degree of exposure, the more certain it is that sensitivity will develop. Once it has developed, it may remain present for years or gradually decrease in severity and finally disappear. Wedroff and Dolgoff¹² carried out some experiments of great significance to industrial dermatology. They were able to sensitize experimentally with one application of 0.03 cc. of 10 per cent dinitrochlorobenzene fifty of seventy-two patients who had had eczema. An incubation period of from eight to twenty-four days was required before the development of sensitization. Sensitivity to this compound increased more than 100,000 times the original degree, and spontaneous regression of sensitivity required from 200 to 360 days. They found that patients with eczema were much more readily sensitized than normal persons, who required 0.3 cc. of a 30 per cent solution of the same compound to produce sensitivity. Repeated applications on patients already sensitized increased the degree and duration of sensitivity. It is apparent that patients with an eczematous eruption are much more easily sensitized to other compounds than are normal persons. This brings us to the question of the selection of workers in industries employing substances with a high sensitizing index.

Selection of Workers.—With few exceptions, one type of skin is just as easily sensitized as another. Certainly a heavy horny layer on the exposed parts is advantageous in preventing penetration of offending allergens. We have not observed that age, or color of skin except possibly in the case of Negroes, is of great importance. In certain industries a dry skin is advantageous. In others a moist skin is just as advantageous. A dry skin is desirable in industries where gases and dusts are present. A moist skin is desirable where liquid irritants are employed. Therefore it is evident that no general statement can be made regarding the desirability of dry or moist skin unless the type of industry is specified.

The preemployment performance of patch tests with substances to be handled in the work is of almost no practical importance. The reason for this is that the worker never reacts to the first contact with a substance. An incubation period, during which sensitization develops, of at least ten to fourteen days is necessary before a positive reaction can possibly be secured. If patch tests are to be used prior to employment, it would be much better to test with a series of ten well known eczematizing agents to determine whether in general the prospective employee has an eczematous tendency. This procedure is of course impracticable in the vast majority of industrial plants. The presence or history of a contact eczema or ringworm is vastly more important than the performance of patch tests. Persons with such a history are more

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liable to acquire other sensitivities than is a normal person, and they should not be employed in industries using substances with a high eczematizing index.

Elimination of Unnecessary Hazards.—Many compounds which have a high sensitizing index can be eliminated in favor of less harmful compounds. Certain oils,¹³ accelerators used in the rubber industry,¹⁴ paint solvents⁸ and soaps and cleaners¹⁵ vary in their tendency to produce sensitization. In order to eliminate the more harmful compounds of industry, it is necessary for the industrial dermatologist and the industrial chemist to cooperate, the former to discover specific causes of an outbreak of dermatitis and the latter to supply a different, less harmful compound which may be successfully used as a substitute.

Special care should be taken when new compounds are introduced in industry. At the first sign of an outbreak of dermatitis, steps should be taken immediately either to prevent contact or to eliminate the substance altogether. In many industries it is absolutely necessary to employ compounds capable of sensitizing a large percentage of the workers. The elimination of these hazards can be accomplished only gradually, by further chemical research. Until they can be removed from industry, the prevention of sensitization must depend on the elimination of intimate contacts between the eczematizing agent and the worker.

Prevention of Exposure to Sensitizing Substances.—There are numerous methods by which prevention of exposure may be accomplished. They have been successfully employed in many industries.

A. Use of closed methods of manufacture.⁵ These methods are of value not only in preventing all forms of dermatitis but also in the prevention of systemic poisoning from the inhalation of dusts and gases.

B. Employment of suitable exhaust hoods to carry off gases, fumes and dusts at their point of origin. In the chromium plating industry,^{4c} employment of exhaust hoods and closed methods of manufacture have almost entirely eliminated cutaneous reactions.

C. Proper general plant ventilation. This is necessary in addition to exhaust hoods to prevent contamination of the general atmosphere.

D. General plant cleanliness. Work benches, walls, floors and pipes should be cleaned frequently to prevent the accumulation of dangerous dusts. Some of our most severe cases of dermatitis have occurred in maintenance men, such as pipe fitters and electricians, who came in contact with dust which had been present for months and years.

E. Proper work clothing. Protective uniforms, including chemically resistant aprons and gloves, supplying the maximum degree of protection, should be issued to all workers handling substances with a high eczematizing index. The frequency of change should depend on the amount of contact in each individual case. These workers should have a complete change of clothing before leaving the plant, and the lockers containing their street clothing should be kept far enough removed from the general workroom so that no dusts can penetrate them.

F. Proper cleansing facilities. Shower baths and sinks should be made available to all workers to permit

complete removal of any potential allergens from the skin. Proper cleansing agents should be supplied. Strong alkaline soaps, lye, turpentine, gasoline and various abrasive cleansing agents should not be used. One observer¹⁶ has stated that he has seen more dermatitis due to the improper use of cleansing agents than to contacts in the occupation. We believe that this factor is extremely important in plants handling substances with a high sensitization index. Cleansing agents should be limited to olive oil, liquid petrolatum and nonirritating toilet soaps.

G. Instruction to workers regarding the danger of their occupation. An intelligent understanding on the part of the workers of the hazards to the skin connected with their work is extremely desirable. Downing¹⁷ has stated that after a lecture the incidence of industrial dermatitis was reduced nearly 75 per cent in a particular plant. It is difficult for workers to understand the mechanism of sensitization. Educational efforts along this line should have a very beneficial effect.

Early Recognition of Sensitization Dermatitis.—One or two weeks of delay in the recognition of a sensitization dermatitis may mean the difference between a dermatitis lasting from two to four weeks and one requiring two or three years to subside. The appearance of a sensitization dermatitis in one worker should lead to closer observation of other workers handling the same substances. Any cutaneous eruption should be reported promptly to the medical department. The plant physician should determine at once whether he is dealing with a dermatitis due to a primary irritant or a dermatitis due to sensitization. If he is unable to decide, consultation should be requested. In our opinion, careful attention to these details would reduce the disability from sensitization dermatitis at least 50 per cent. If the eruption is a sensitization dermatitis, no matter how mild, the worker should be sent home and should remain there under treatment until the skin has completely healed. When he returns to work he should be assigned to another job, handling entirely different substances, with a low eczematizing index.

The question of first aid treatment of industrial dermatitis is extremely important. All too often ointments, lotions and sprays are applied which in themselves are highly eczematizing. We refer particularly to the widespread use of butesin picrate, ammoniated mercury, tannic acid sprays containing mercurials, and many other proprietary remedies found in some first aid rooms. Some of our most severe and distressing cases of industrial dermatitis have arisen from the injudicious use of these preparations. In our opinion, there is no necessity for the employment of any highly eczematizing substance in first aid work. Simple wet dressings, lotions and ointments are all that is indicated.

OTHER OCCUPATIONAL DISEASES OF THE SKIN

Diseases of the pilosebaceous apparatus arising as a result of occupation, i. e. acneiform eruption, comedones and furuncles, are commonly encountered in workers in oil,¹⁸ paraffin,^{18b} lubricating compounds,^{18c} chlorine compounds,² sugar¹⁹ or hypertonic salt solution.^{18a}

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McConnell^{18c} found that 27 per cent of 557 workers whose occupation required exposure to cutting oils and lubricating compounds had oil acne. The condition is apparently due to simple mechanical blocking of the hair follicles with oil and foreign particles in the oil rather than to the presence of some infectious agent. The addition of antiseptics to oil or sterilization of oils by heat has not succeeded in cutting the incidence of this condition.^{18c} Rosenberger²⁰ made bacteriologic studies of cutting oils and found staphylococci or streptococci only rarely a contaminant of either new or used oil. All who have studied this problem are in accord that cleanliness is of the greatest importance in the prevention of this common dermatosis. This consists in frequent washing of the exposed parts and frequent change of clothing. The use of lotions, powders and vegetable oils has proved of value in some instances. The use of protective pastes has proved of practical value.

Occupational Keratoses and Cancer of the Skin.—These conditions are common in workers in paraffin,^{18b} pitch,²¹ certain oils²² and arsenic.²³ Keratoses usually precede the development of epithelioma. The Tworts²⁴ pointed out that certain oils are more carcinogenic than others. The highly hydrogenized oils are the least dangerous. Oils from certain parts of the world are more carcinogenic than others, and this apparently depends on the degree of hydrogenation. Mineral oils employed in the English textile plants are much more carcinogenic than the vegetable oils used in American textile plants. The Tworts pointed out that carcinogenic oils can be commercially treated to make them less dangerous. It is self evident that all workers handling carcinogenic agents should be frequently examined for keratoses and that if such growths are present they should be removed. Frequent and thorough cleansing of the skin and the use of protective ointments and pastes are indicated.

Cutaneous Anthrax.—Anthrax still remains an occupational hazard among the handlers of hides, hair and wool.²⁵ In the majority of cases the condition arises from the handling of infected hides imported from some country in which laws regarding the disposal of infected animals are not rigidly enforced. Since chemical disinfection of hides is unreliable²⁶ there is only one method of prevention of this severe disease, and that is the placing of an embargo on all hides imported from countries which do not have stringent laws regarding the proper disposal of animals dying from anthrax. Infection from American hides is rare because practically all states rigidly enforce the regulations.

CONCLUSIONS

1. Industrial dermatoses to a large extent are preventable. To bring about prevention, scientific facts now available must be utilized.

2. Industrial dermatitis is the most common and important cutaneous hazard. There are two types: (a) dermatitis due to primary irritants and (b) sensitization dermatitis.

3. The prevention of dermatitis due to primary irritants depends on two factors: (a) mechanical means of protection and (b) education of the workers.

4. The prevention of sensitization dermatitis depends on (a) the proper selection of workers, (b) the elimination of unnecessary hazards, (c) the prevention of exposure to sensitizing substances and (d) the early recognition of sensitization dermatitis and its proper management.

5. The prevention of industrial diseases of the pilosebaceous apparatus consists essentially in personal cleanliness and the use of suitable protective measures.

6. Occupational keratoses and cancer of the skin may be prevented by (a) personal cleanliness, (b) the use of suitable protective measures, (c) the use of non-carcinogenic oils and (d) the prompt removal of keratoses.

7. The prevention of anthrax depends largely on the rigid enforcement of suitable sanitary regulations.

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ANALYSIS OF CLAIMS IN INDUSTRIAL DERMATOSES

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An analysis of the component parts of claims for compensation for occupational dermatoses includes consideration of all problems related to the differential diagnosis as between the cutaneous disease arising from natural causes and that due to occupational hazards. This may necessitate considerable research in addition to a thorough physical examination, extensive clinical laboratory work, thorough investigation of the industrial exposures, and knowledge of the legislation of one's state as to dermatitis, the local insurance coverage, the mode of procedure of its deciding power and preceding decisions of commissions, medical boards or courts. A dermatologist should be cognizant of these subjects even if he does not care to do industrial work; in fairness to his patients he should be able to diagnose eruptions due to occupation and to advise his patients properly as to their further care and welfare. His training should enable him to diagnose eruptions arising from natural causes; as to occupational eruptions, Stauffer¹ demonstrated that it is possible to show the exact cause in nearly all cases, although in actual practice this result is not possible, for essential proof is often lacking. Experience in similar cases and study of the hazards, the mode of onset and the resulting physical signs will result in a decisive opinion in the large majority of cases, but there will remain a small group of cases in which the cause is undetermined and disputed and must be settled by an industrial accident board.

This analysis will be confined to the procedure in Massachusetts, where, as provided in the Workmen's Compensation Act, seven lay members comprise the Industrial Accident Board. It has been proposed that cases involving industrial dermatoses should be decided by medical men, but persons who favor this idea do not realize the large number of cases that are in fact

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22. White.² Schwartz.^{18b}

23. White.² Bridge.²¹

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judged by dermatologists. Dermatologists receive cases early and review them carefully. If the dermatologist concludes that the disease is nonoccupational, he explains this to the claimant, who in most instances is an honest worker and is relieved to know that his occupation is not to blame; if the dermatologist believes the disease to be occupational, he so informs the insurer, giving his reasons in full. The insurer rarely disputes the finding of a trained dermatologist, whether or not he selected him. The result is that hearings on occupational dermatoses are few in comparison with the number of cutaneous eruptions appearing in workers. In 845 of a series of 2,000 claims examined privately for insurers the dermatosis was considered nonoccupational; in 1,004 it was considered occupational, and in 151 it was not diagnosed. The diagnosis was contested in only 3 per cent of the cases. The dermatologist can always secure further medical assistance by consultation before rendering an opinion if he so desires, so that the medical aspects of the case may be assumed to have been thoroughly investigated. No one is better qualified to decide the diagnosis, the differential data and the etiologic factor than are dermatologists; when they disagree an impartial and duly qualified dermatologist is appointed to examine and report, and his report is considered admissible as evidence provided the employee and the insurer have been seasonably furnished with copies of it (General Laws, chapter 152, section 9). The employee who is unable to employ a dermatologist always has the right to an impartial examination. Payment is made by the board, although the law requires the insurer to reimburse it. The impartial dermatologist is usually given all the facts in the case, a summary of any hearings that have been held and all medical reports. Impartial physicians have been summoned to hearings of the Industrial Accident Board by either the plaintiff or the defendant, but to date the board has ruled that they should not be subjected to cross examination and has refused to allow them to testify. There has as yet been no court ruling on this decision.

On Oct. 14, 1935, the appointment of three physicians, to be known as industrial disease referees, whose final diagnosis is binding on both parties, prompted me to suggest the use of the term *ergodermatosis*² for the diagnosis of cutaneous eruptions arising out of and in the course of occupation (General Laws, chapter 152, section 9B). The diagnosis of these medical referees must be made on the physical signs present at the time of examination, although this diagnosis may be made months after the onset, perhaps when the patient has recovered. As a result, interesting complications are already developing.

With the etiologic factors decided and the diagnosis made, it may be asked why a lay board is needed. The answer is that the administrators of the compensation act need more than medical knowledge, for legal puzzles arise daily, the credibility of witnesses must be evaluated and working conditions and labor problems must be considered. With this in mind, the framers of the act wisely decided that the board should consist not of physicians or lawyers but of laymen; their decisions when reasonable and sensible are usually supported by the courts.

The Massachusetts Workmen's Compensation Act was designed for the protection of employees injured in occupation and to offset the advantages given to the

employer under the common law, whereby the worker had to prove negligence on the part of his employer. It went into effect on July 1, 1912. One of the first questions to be settled was whether occupational diseases were covered by the act. It provides for compensation only for a personal injury arising out of and in the course of employment (*Minus Case*, 286 Mass. 459). It affords no remedy for disease, occupational or otherwise, contracted in the course of and arising out of employment. The construing of the words personal injury is left to the court. The court said in the *Burn case* (218 Mass. 8):

"Injury," as applied to a personal injury to a human being, includes whatever lesion or change in any part of the system produces harm or pain or lessened facility of the natural use of any bodily activity or capability.

In the *McNichol case* (215 Mass. 497) the court said:³

It is sufficient to say that an injury is received "in the course of" the employment when it comes while the workman is doing the duty which he is employed to perform. It "arises out of" the employment when there is apparent to the rational mind, upon consideration of all the circumstances, a causal connection between the conditions under which the work is required to be performed and the resulting injury. Under this test, if the injury can be seen to have followed as a natural incident of the work and to have been contemplated by a reasonable person familiar with the whole situation as a result of the exposure occasioned by the nature of the employment, then it arises "out of" the employment.

In other words, this is a rational law, to be administered by reasonable persons in a practicable manner for practical people, and has been so executed by the Industrial Accident Board. The compensation payments are made promptly, and when disputes arise hearings are assigned quickly and decisions are made without delay. While mistakes occasionally occur, they are few when one realizes the responsibility and magnitude of the board's task. Every day presents new problems and questions, as shown by the following cases:

CASE 1.—*G. P. M. v. T. Mfg. Co.* Hearing Oct. 19, 1931. The patient worked three and one-half years as an electroplater, coming in contact with potassium cyanide. An eruption appeared on his hands three months after he started to work and remained until he stopped work because of his dermatitis, loss of weight and weakness. Two physicians called by him testified that he had been disabled as a result of his employment. Two physicians called by the insurer believed that his work had nothing to do with his disability, having seen him after his cutaneous condition had disappeared. The impartial dermatologist reported that the cutaneous condition was due to the cyanide used in work. The board member's decision, based on the impartial opinion, stated that, as the medical testimony at the hearing was neither decisively for nor decisively against the contention of the employee, he had sustained an injury arising out of and in the course of his employment, with resulting total disability. With contradicting medical testimony, the commissioner is apt to base part of his decision on the impartial report, especially if there has been exposure to irritants. In this case the insurer introduced the foreman of the plating department, who testified that the employee had had very little contact with the silver solution and chemicals used in the work. However, the employee testified very clearly that he used potassium cyanide every day that he worked. The member said, "I believe that the employee himself was in the best position to know the extent of his exposure, and I accept his testimony on that point."

2. White, R. Prosser: *The Dermatogoses*, ed. 3. London. H. K. Lewis & Co., Ltd., 1928.

3. Granfield, Robert E.: *Workmen's Compensation Administration in Massachusetts*, the *Annals* 126: 66-74 (March) 1928.

The board does not, however, always accept the employee's opinion when there is sufficient evidence against the presence of irritants in the employment:

CASE 2.—*E. B. N. v. T. Spa.* Hearing Aug. 23, 1930. The patient, a counter girl and waitress, claimed that she had an eruption on the fingers of both hands as the result of constant wetting of her hands for eight hours daily. Her own physician, a dermatologist called by the insurer and the impartial examiner diagnosed her condition as epidermophytosis. Her employer at the hearing showed that there was no necessity for any constant wetting of the hands, her work being of a clean, dry type. The member decided on careful examination of the evidence that the employee had failed to prove that her incapacity was the result of her work.

A fungous infection of the skin is considered a disease, and not caused by industrial contacts, and if there is no evidence of irritants in the work which would aggravate this disease, the patient has little support for his contention that such were present:

CASE 3.—*I. B. v. J. N. Co.* Hearing March 3, 1930. The patient stated that she had worked for five and one-half years as a salesgirl, selling art goods, yard goods and hardware, and that as a result of the occupation she suffered an eruption on her hands. The diagnosis by her own physician and by a dermatologist was epidermophytosis. The claim for compensation was dismissed because her eruption was considered non-occupational and because there was no satisfactory evidence that it was aggravated by her work.

While a fungous infection of the skin is considered a disease rather than an injury, when working conditions are such that they might aggravate the disease the board recognizes this fact in its decision:

CASE 4.—*C. C. v. G. E. Co.* Hearing Nov. 21, 1930. The claimant, a wet grinder, stated that water leaked out of his machine, causing his feet to become saturated with a solution containing 11 pounds (5 Kg.) of soda to 50 gallons (200 liters) of water. He worked under these conditions until he suffered such a severe pain in one foot that it was necessary for him to stop work. The plant physician diagnosed his condition as epidermophytosis, not occupational, but on cross examination admitted that a wet stocking might have irritated the eruption on his foot. His own physician stated that he had a dermatitis due to an alkali. In this case the member decided that the employee had received an injury arising out of and in the course of his employment. The insurer filed a claim for review of the decision, and a reviewing board of three members affirmed it.

The mere fact that a patient is compensated for an eruption occurring during employment does not necessarily mean that he will be compensated for later eruptions if testimony shows that he does not come in contact in his work with irritants which could cause or aggravate a dermatitis:

CASE 5.—*M. D. v. H. R. Co.* Hearing May 1, 1933. On Aug. 16, 1929, the patient became disabled from a fungous infection which she thought was aggravated by contact with naphtha at her work. The insurer denied that the condition was caused or aggravated by her work but agreed in the absence of a specific diagnosis to pay the employee against her further rights and accordingly paid compensation from Aug. 16 to Dec. 6, 1929. The patient then returned to her work of lacing shoes, at which time the eruption had not entirely cleared. The diagnosis of the plant physician and two dermatologists was epidermophytosis. The impartial report, which was not read at the hearing, must have disagreed with this, for the defendant's lawyer summoned the impartial physician, his reason being that this physician's opinion was based entirely on the history given by the employee, which the insurer alleged to be false. The member ruled that the impartial examiner should not have been forced to appear and therefore did not allow him

to be cross examined. From the history of the work and from medical testimony the member decided that the patient had failed to prove that any disability from which she suffered from Feb. 15, 1932, was related to the injury which she sustained on Aug. 16, 1929, and her claim for compensation was dismissed.

Medical bills are handled by a majority of the board as a whole. The evidence is taken by a single member, but he does not make the decision alone:

CASE 6.—*R. C. T. v. W. G. F. Shop.* Hearing Sept. 8, 1930. The claimant, a florist, suffered an eruption on his hands from contact with plants; his statement was confirmed by his own physician, the hospital clinic and a dermatologist, and he was awarded compensation. His medical bills were protested as excessive, but four members decided that he had a stubborn outbreak of dermatitis which required the services of a specialist. The board found that this case came within the meaning of General Laws, chapter 152, section 30, according to which the board may in its discretion approve the payment of services beyond the first two weeks and approve for payment by the insurer the bills of the dermatologist and also of the general practitioner.

A patient with impetigo contagiosa may require considerable proof before he is satisfied that his condition is not occupational:

CASE 7.—*J. R. v. W. F. Sons Co.* Hearing Feb. 4, 1935. The patient claimed to be disabled as the result of acquiring impetigo from handling fur coats. The only evidence was that of a dermatologist, who stated that the patient had impetigo contagiosa, which was not in his opinion occupational. The member agreed with this opinion. The plaintiff appealed to a reviewing board, which also dismissed the claim.

The board is fairly well agreed that certain diseases of the skin are not compensable. However, every now and then a member surprises every one by awarding compensation to a claimant who is suffering from a recognized nonoccupational cutaneous eruption:

CASE 8.—*F. J. McN. v. A. Prod. Co.* Hearing June 4, 1934. The claimant, a molder, claimed that the cause of his cutaneous eruption was the excessive heat and dust with which he came in contact while making bakelite fittings. His physician diagnosed his eruption as "erythematosis" due to the excessive heat and dust. Two dermatologists agreed that it was psoriasis; and one stated that it was in no way related to his work, and the other stated that in his opinion it was not occupational but that he could not say that the work did not cause it. With this in mind and with the knowledge that bakelite workers are subject to cutaneous eruptions, the member awarded compensation to the claimant and ordered the insurer to pay reasonable bills, which, as one would expect, were rather large. In this case there was no evidence of any industrial dermatitis, despite the fact that the type of work may produce an eruption. Here is a case in which a man, although engaged in an occupation hazardous to the skin, presented an eruption which was known many years before the discovery of bakelite and which certainly belongs in the nonoccupational class.

If there is a history of injury outside of employment, compensation is apt to be refused although the patient is exposed to possible sources of infection:

CASE 9.—*G. W. v. W. H. S.* Hearing Dec. 9, 1921. The claimant, an undertaker's assistant, suffered a severe infection of his face, with resulting osteomyelitis of the jaw, which, he stated, was due to an infection acquired at his work. The claimant said that he believed that the infection started soon after he cut his chin with a razor while shaving. Although he contended that the infection was acquired in the course of his work, which brought him in contact with diseased bodies, it was found that he had not proved that the infection and the incapacity caused thereby were related to an injury arising out of and in the course of this employment. His claim for compensation was dismissed.

However, if a patient definitely shows that he suffered an injury at his work and then acquired an infection, compensation is generally awarded:

CASE 10.—*T. N. v. H. R. Co.* Hearing May 17, 1932. The patient, engaged as a cementer of rubber soles, while doing this work suffered an eruption on his left thumb. He was treated at the plant clinic, where a diagnosis was made first of eczema and then of ringworm. He then suffered a severe infection of his thumb, with resulting septicemia. At the hearing the plant physician maintained that the irritants which were previously present in the rubber cement, namely hexamethylene-tetramine (called "hexa") and dinitrophenyl dimethyl dithiocarbonate (called "safex") had been removed and that the cement was no longer a hazard to the skin. He stated that he believed that the man's disability resulted from a fungous infection and was not related to his work. A dermatologist who appeared for the employee testified that he had had a felon of his thumb, with resulting septicemia, and not an industrial dermatitis. Another dermatologist called by the employee testified that in his opinion the disability arose primarily from a dermatitis of the thumb caused by the cement, which later became secondarily septic, and that the injury therefore originated from his work. The member, in summarizing his decision, based it on the fact that the man was treated for a long time at the employer's clinic, where a diagnosis of eczema was made and was later changed to one of ringworm. He felt that a fair preponderance of the evidence showed that the patient had suffered a disability brought about by his work. He therefore awarded him compensation for a period of thirty-eight weeks.

If a claimant reports an injury at his work and it later becomes septic, he will receive compensation:

CASE 11.—*A. N. v. P. S. Co.* Hearing June 8, 1921. The patient, a heel liner, stated that a tack became stuck in the back of her right hand; the wound became infected, with the result that she suffered a severe infection of her hand and arm. This was confirmed by her own physician, and she was compensated for a period of two and one-half months.

When sepsis complicates a dermatitis, the insurer is apt to regard this condition as nonoccupational, although the same insurer will without complaint pay a claimant suffering from sepsis following a wound:

CASE 12.—*F. C. v. W. T.* Hearing Feb. 24, 1933. The claimant, employed as a cook and dishwasher, suffered a dermatitis of his hands, but he continued to work, and while doing so it was necessary for him to clean fish and open lobsters. A septic condition then developed, with lymphangitis, which necessitated his stopping work. His own physician stated that he had no definite opinion as to the cause of the condition. His employer admitted that the man suffered from burns on his hands from hot grease, cuts on his palms from handling lobsters and an eruption from contact with soap powders. The impartial examiner stated that he believed that the infection started from dermatitis venenata. The member found that the employee was disabled as a result of an injury arising out of and in the course of his employment and awarded him compensation for five months' disability.

At times it is difficult to decide which insurer is liable for compensation:

CASE 13.—*T. C. v. A-L T. Co.* Hearing Jan. 29, 1931. The claimant, a seasoner of leather, suffered a dermatitis while working for a tanning company. The eruption appeared on both hands and forearms. He stopped work May 2, 1930, and was compensated to May 21, at which time he signed an agreement of discontinuance but testified that he still had an eruption on his hands. The presence of an eruption was confirmed by his physician. In July he went to work for another leather company but stopped at the end of a week and a half because of a dermatitis of his hands. As his hands were not well at the time of this last employment, the commissioner found the insurer of the first company liable for payment of his compensation, which was granted from May 25 to Sept. 29, 1930, except for the week and a half that he worked. The outbreak

from work at a second factory was considered a recurrence of his former condition and not a new injury. This man was advised not to return to his previous trade and was granted partial compensation. He was advised to accept work at a lower wage, and the partial award was made to compensate him for the diminution in earning capacity. The insurer appealed the case, but a reviewing board affirmed the member's decision.

When a man is disabled from contact with irritants and his eruption is relieved, he is generally advised not to return to his previous occupation. If he neglects this advice, he is apt to be refused compensation:

CASE 14.—*J. K. v. M. S. Co.* Hearing Oct. 29, 1930. The claimant, an assembler of shoes, suffered a dermatitis due to handling a new paste on an assembling machine, for which he received compensation. His case was assigned for a hearing at the request of the insurer in order to determine the amount of disability, if any. According to the insurer's physician, the man's dermatitis was relieved. It had been shown that he was very sensitive to the paste, and he was aware of this fact, for it had caused a recurrence of his eruption on the slightest contact. However, four days before the appointed hearing he returned to his old employment, came in contact with the same paste and suffered a prompt outbreak of his dermatitis. Just before returning to work he had been seen by an impartial physician, who stated that his hands were perfectly normal and advised him not to return to contact with the paste. The member decided that the claimant had recovered entirely, that he had been warned by his physician not to return to his former work or to expose himself to the paste which had caused his trouble, and that his doing so was a "voluntary act on his part," which broke the line of causation between his original injury, arising out of and in the course of his employment. The insurer was authorized to discontinue compensation.

When a patient receives treatment for an industrial injury and then suffers any subsequent incapacity as a result of this treatment, he is eligible for compensation:

CASE 15.—*J. G. v. C. S.* Hearing April 20, 1927. The claimant, while digging in a trench, dropped a pick into some electrical equipment in a cement box and received an electrical shock. The accident left him in an extremely frightened state of mind, with the result that a neurologist prescribed bromides in fairly large quantity. Later he suffered an outbreak on his lower legs. The report of the impartial examiner stated that the claimant was suffering from an eruption on his lower legs due to bromides. He was awarded compensation for a period of nineteen weeks.

Treers, men who clean, dress and iron shoes, are well paid but as a rule are not employed steadily. They are apt to suffer a dermatitis while employed at one company and to work until there is a lay-off; they then claim disability, return to work before they are entirely relieved and have another outbreak. The insurers try to dispose of the cases by payment of a lump sum, but this does not prevent a worker from collecting from another insurer for an eruption acquired at a different place of occupation:

CASE 16.—*M. M. v. H. S. Mfg. Co.* Hearing Aug. 8, 1932. The claimant, a shoe treer, worked for the P. Shoe Company and suffered a dermatitis, for which he was compensated for six months by the Z. Insurance Company. He went to work for the F. Shoe Company, suffered a dermatitis and was paid compensation by the G. Insurance Company. He then went to work for the D. Shoe Company and was paid compensation by the A. M. Insurance Company in a lump sum. He then went to work for the H. Company and had another outbreak. He stated that each time he returned to work his skin was well. In this case there was no evidence brought out that any one had forbidden him to return to his trade, so that the point referred to in the previous case does not always hold true. The member found that the man was totally disabled as a result of his last attempt to work and awarded him full compensation. (It is

my belief that the previous attacks were paid for because the man suffered on each occasion a dermatitis of short duration and the insurance company found it cheaper to pay his compensation than to bring the case to a hearing. There is no evidence of any hearings except this one.)

If a man suffers a dermatitis which finally clears, he is inclined to attribute all subsequent conditions to it:

CASE 17.—*J. K. v. B. Shoe Co.* Hearing April 24, 1931. The patient, a treer, suffered a dermatitis for which he received compensation until his eruption had disappeared. Later he complained of a tremor of the hands, which he attributed to his previous condition, claiming further compensation. His own physician testified that the tremor was the result of his dermatitis. A dermatologist was of the opinion that there was no relationship, and every one at the hearing was able to note the increase of the tremor each time attention was called to the patient. This fact was evidently noted by the member, for he dismissed the claim.

It is at times very difficult to decide whether or not an employee is disabled; a condition with which a man has been able to work suddenly becomes very disabling when there is a lay-off:

CASE 18.—*N. S. v. P. Shoe Mfg. Co.* Hearing Dec. 2, 1935. The patient, a treer, claimed disability as the result of a dermatitis on one finger. While a treer may have some difficulty in working with an eruption on one finger, he is not totally disabled. The claimant stated that his right second finger became irritated from cleaning shoes. He continued to work, however, until he suffered in addition a dermatitis on the right thumb. He then stopped work. It was agreed that he had an occupational dermatitis and he was advised to return to work. He did so and worked until he again had an eruption on his fingers. At that time there was a lay-off. His physician testified that his eruption was relieved and that he advised him not to return to the work of dressing shoes because of susceptibility. The impartial examiner agreed with this opinion. The member granted him compensation but recommended that he wear a finger cot and make a further effort to do his work. He was granted fifteen weeks' compensation up to the date of the hearing. This was paid by the insurer without protest, but a full board was required to decide that the treatment given him by his physician was necessary.

In other cases the employee may be refused compensation and the physician be paid without protest:

CASE 19.—*A. C. v. T. G. P. Corp.* Hearing Nov. 17, 1931. The patient suffered a dermatitis while working for the P. Shoe Company as a shoe cutter but was able to work until the firm finally went out of business. He did not report his injury. In the meantime his dermatitis quieted down. He went to work for the C. Shoe Company doing the same work and was employed there for about six months, until there was a lay-off. Medical testimony agreed that he had an industrial dermatitis. However, the claim was made against the insurer of the P. Company, and the member decided that the patient's incapacity, if any, was due to exposure at the time he was employed by the C. Shoe Company. Since there was no claim made against the insurer of this company, the member made no finding as to the payment of compensation. A second hearing was held on June 14, 1932, against the insurer of the C. Shoe Company. The medical experts were then confronted with the problem of deciding whether the dermatitis was a result of the injury sustained at the P. Shoe Company or whether there was an intervening lapse of relief, with an acute exacerbation from the patient's second employment. A dermatologist called by the employee testified that it was a new injury and disabling. A dermatologist called by the insurer stated that at no time had the man suffered from a disabling dermatitis. Both recommended treatment. It was ruled that if the employee did have a dermatitis his present condition was a new injury but that there was no incapacity for work as a result of this injury and therefore he was not entitled to any compensation. The recom-

mendation was made, however, that he be treated. The man returned to work and continued at it for five years without any disturbance. In 1937 he came in contact with white buckskin, which out of twenty leathers was the only one to which he was sensitive, and suffered a dermatitis which disabled him for several weeks.

The onset of an industrial dermatitis frequently becomes a debatable point. While it is usually recognized that the date of the injury is the time when disability begins, occasionally when a new insurer takes over a risk and the employee then becomes disabled, the compensation may be divided between the two insurance companies:

CASE 20.—*J. H. v. J. G.* Hearing April 18, 1929. The claimant, a lithographer, suffered a dermatitis from contact with inks, oils, kerosene, turpentine and chromic acid, which started in June 1928, but he did not stop work until November 1928. During all this time the eruption persisted, growing progressively worse, until he was totally incapacitated on November 17. On November 1 a new insurance company took over the risk, so that the commissioner found that the two companies were jointly liable. This decision was affirmed by a reviewing board. This finding will probably not be made again because of the supreme court decision in the Donahue case in 1935 (290 Mass. 239), in which the board found that the pneumoconiosis in question was due to accumulative exposure over a long period, but that the insurer who covered the risk at the time the disability occurred was liable. The insurer appealed to the court on the ground that one or more of the previous insurers should contribute. The court said "It is significant, however, that none of our decisions give any support to the suggestion that several insurers can be held jointly. We think the implication from the statutes and from all the cases taken together is so strongly against the appellant that the question cannot fairly be said to be still open."

A point which is frequently brought in is susceptibility. The decision in 286 Mass. 541 (1934) is authority for the statement that when the original eruption had cleared up but the "skin had never returned to normal" there was "disability as to the particular employment (involving exposure) but not as to employment in general" and "it was the duty of the employee to try to get other work":

CASE 21.—*R. C. v. D. Mfg. Co.* Hearing Jan. 5, 1933. The claimant, a machine worker, came in contact with various dyes. Medical testimony agreed that he had suffered a dermatitis. The patient worked with the dermatitis until he was laid off. His eruption then disappeared. Since then he had not worked because he did not dare to come in contact with irritants. A dermatologist called by the employee admitted that the dermatitis had cleared up but said that he should not resume work which would bring him in contact with chemicals. Although this situation was admitted, the member ruled that mere susceptibility did not constitute disability. This opinion was supported by a reviewing board. At a previous hearing this man had been awarded total compensation from April 1931 to September 1931 and partial compensation to Dec. 16, 1931.

CASE 22.—*M. D. v. R. Preserving Co.* Hearing May 2, 1928. Removing stones from dates can cause a dermatitis, testified by two dermatologists in this case. This decision was confirmed not by patch testing but by the evidence that each time the claimant returned to this work she suffered a new outbreak, although she could do other types of preserving without infection.

Bakers' eczema is very persistent and is apt to recur. Some employees are so anxious to return to work that they are willing to sign away their rights in order to secure employment:

CASE 23.—*R. N. v. R. G. S. Co.* Hearing June 29, 1933. The claimant, a baker, suffered a dermatitis while employed at the bakery and received compensation. He then requested work at his place

of employment and signed the following statement: "I, R. N., will not hold the R. G. S. Co. responsible for disability resulting from any condition to my skin through my occupation as baker with them." It was agreed that this man had bakers' eczema, and while the insurer told the employer not to employ him there was no medical testimony forbidding him to return to the work. Despite the signed statement, the member ruled that this had no legal effect on the employee, since it was not a waiver within the terms of the statute, and that when the employee was compelled to stop work on account of his dermatitis he sustained a recurrence and was therefore entitled to compensation. This decision was confirmed by a reviewing board.

If a claimant presents proof that he has been told that he can return to his former occupation, the supreme court decision forbidding such an act does not apply:

CASE 24.—*W. T. v. 80 F. Street Restaurant*. Hearing June 11, 1934. The claimant, a baker, did ordinary hand mixing and suffered various outbreaks on his hands from 1929 to 1934 because of his occupation. In 1932 he had received a lump sum settlement for a similar dermatitis due to this work. At that time a dermatologist who treated him told him that he could return to his work. There was no question as to his dermatitis or disability, but the question of its being a recurrence of the condition from which he had suffered in 1929 was raised by the insurance company. However, he stated that when he went to work in 1933 for the company involved his hands were perfectly well and that he worked for six months without trouble. Because of his testimony, in which he stated that he had been told that he could return to his work, it appeared that he was justified in thinking that it was all right for him to do so. He was therefore awarded compensation.

The presence of active lesions of syphilis does not bar an employee from compensation if there is evidence of an industrial dermatitis:

CASE 25.—*v. K. J. Q.* Hearing June 29, 1931. The report of the impartial examiner stated that the claimant had an industrial dermatitis on his hands and forearms but that there were active lesions of syphilis, which were confirmed by serologic tests. The syphilis was not in any way related to his occupation. He was awarded compensation for his industrial dermatitis, irrespective of his constitutional disease.

When an employee is housed as part of his employment he is apt to make a claim for eruptions following exposure to parasites:

CASE 26.—*W. O. v. O. H. Inc.* Hearing Dec. 4, 1926. The patient testified that as part of his employment he was compelled to sleep in a bed furnished by his employer and that shortly afterward he suffered from itching all over his body. A diagnosis of scabies was made by a dermatologist. The claimant gave no proof that others were so affected, and the member dismissed his claim.

A claim for compensation is supposed to be made within six months of the injury. However, the late filing of a claim does not prevent the payment of compensation if the member decides that the insurer was not prejudiced. If the employer has knowledge of the injury at or reasonably soon after the happening thereof, tardiness in filing a claim is excused. The same is true if the tardiness does not prejudice the insurer's right to investigate or treat the condition. No element of fault on the part of the employer seems to be involved. *Crowley Case*, 287 Mass. 367 (1934), and *Hatch Case*, 290 Mass. 259 (1935).

CASE 27.—*F. Q. v. D-G Kid Mfg. Co.* Hearing June 1, 1931. The claimant suffered a dermatitis on Oct. 22, 1929, but did not file a claim for compensation until June 1, 1931. His work consisted of stacking leather, and he came in contact with wet skins, recently tanned. His physician testified as to

his having an occupational dermatitis. When he was questioned as to why he did not file a claim sooner, he testified that he had expected some one to tell him about it. However, on Nov. 23, 1929, he notified his employer that he could not work because of his condition. He was awarded compensation, provided the member found that the late filing of the claim had not prejudiced the rights of the insurer. The claimant was compensated from Oct. 23 to Dec. 9, 1929. It is interesting to note that the man returned to the same work and apparently had no recurrence.

Another example of late filing of a claim is one that occurs when the employee is uncertain as to what work caused his final disability:

CASE 28.—*T. C. v. W. Co.* Hearing Feb. 9, 1923. The patient filed claims for compensation against three different companies. It was brought out that he first had trouble with his hands on Dec. 30, 1920, while working for the W. Company, where he was employed for five days. He continued to work for this company, doing various jobs, and continued to have a dermatitis. A strike threw him out of work from January until May 20, 1921, and during that time his dermatitis was relieved. In August 1922 he went to work for the N. W. Company, which was insured by a different company, and again suffered a dermatitis of his hands, which persisted. He then went to work for J. H. D., who was insured by a third company. At that time he still had a dermatitis of his hands, which increased at his work, so that finally he had to stop work on Dec. 8, 1922. At that time he went to a local hospital, where he learned for the first time that his trouble was due to his work. He then filed claim for compensation against the three companies. He was seen by two dermatologists, who agreed that he had an industrial dermatitis. From the evidence in this case the member found that the employee while in the employ of the W. Company had received a personal injury which consisted of an eruption on his hands caused by contact with cement, that this dermatitis disabled him from Dec. 8, 1922, to the time of the hearing and that he was still totally incapacitated. The member decided that the man did not definitely know until Dec. 20, 1922, that his injury was caused by cement and therefore had a reasonable cause for not filing a claim for compensation before this time. It was found that the employee filed his claim within a reasonable time after he had learned the cause of his injury.

These cases show that medical knowledge, while of value, is not essential, for it may be entirely disregarded. The board member learns to evaluate both the opinions and the physicians expressing them and to accept or reject the opinions accordingly.

The word of a qualified dermatologist has considerable weight with the board, but how are the members to judge the qualifications of the newcomers appearing before them? A list of "diplomates" certified by the national examining boards would solve this difficulty, for certification would at least establish that the physician was able to distinguish eruptions arising from natural causes from those coming from occupation. There would be less attribution of cutaneous diseases of unknown origin to industry, especially those recognized long before the industry in question came into existence. The same care should be exercised in establishing the diagnosis of an occupational disease that is used with nonoccupational ones; and, apart from the contagious group of the latter, the former are of greater importance, for more people than the worker himself are affected. The exposures must be studied and the differentiation must be made between a hazard, carelessness and an idiosyncrasy. What might be a hazard to one worker is not necessarily one to a group, so why change a whole process when the employee can be put on other work? In one case I made an inspection of a plant with another physician, who decided

that twenty skilled mechanics should be laid off because of a persistent dermatitis of the fingers. This lay-off meant the shutting down of the plant, with hardship to over 200 employees. On my advice it was decided to keep these twenty men at work. They continued to work without difficulty, and some were relieved without change of occupation. When a dermatitis occurs regularly in a given occupation and presents characteristic signs, undoubtedly it is occupational. Not every outbreak of eruptions in a plant, however, is necessarily occupational, any more than is an outbreak of impetigo in a classroom, and a careful inspection of the plant and employees will reassure both the employer and the workers.

In the case of occupational dermatoses the irritants should be pointed out and modified or eliminated, or else protective measures should be installed. If the disease is nonoccupational, this should be explained to the employee, who should then be referred to his physician. If his condition is contagious he should be sent home until relieved. Nothing hurts the morale of a plant more than the suspicion of a hidden hazard, and the dermatologist, when called, should be familiar not only with the poisons which cause local cutaneous disturbances but also with those which have systemic effects, for the skin may be the alarm which warns of an unsuspected poison. Nevertheless, the importance of occupational dermatoses must not be exaggerated by elaborate figures. Dermatitis venenata in ordinary life, while it may present an occasional serious eruption, is not viewed with alarm. The patient when told this is reassured and either carries on his activities or resumes them after a short period without ill effects. The same is true of the majority of occupational eruptions. The serious ones are those which show that there has developed a sensitivity to a certain trade chemical which means the loss of the occupation and those in which there is present a poison which causes severe systemic disease, such as benzene poisoning, which may not be recognized until hemorrhagic lesions have appeared. Germ diseases, with the exception of anthrax and the occasional primary fungous infections, are few. While dermatitis is the chief cause of compensation claims in most states, careful study of these claims rules out many of them.

In New York in 1936, of 1,036 claims, 684 (66 per cent) were for dermatitis, of which 299 (29 per cent) were allowed. Occupational dermatoses are so apparent that means for their prevention can be more easily adopted than is the case with any other group of occupational diseases, and if the dermatologist has the necessary training and interest and is cooperative, industry will naturally turn to him in its problems. With the recent inclusion of occupational dermatoses in the compensation laws of some states, the dermatologist has assumed a new function in appearing before industrial commissions; he should be extremely careful as to his opinions and testimony and should not allow himself to be called in merely to cast doubt in a particular case. He should exercise the greatest care in the examination and study of each claimant before expressing an opinion, so that he may be able to support his diagnosis against clever legal cross examination. If, however, there are presented at the hearing new facts which prevent him from conscientiously adhering to his previously expressed opinion, he should admit his error. Otherwise expert dermatologists will have their opinions

cast aside, as in some of the cases reported, and will soon be discredited, with the resultant appointment of state medical officers in their place. This is especially likely to occur if the costs of compensation enlarge until industry can no longer pay them and the state assumes the burden.

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THE COMPENSATION LAWS AND RELATED MEDICOLEGAL CONSIDERATIONS

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Industrial or occupational dermatoses have received recognition as distinctive and important diseases of the skin not alone on account of outstanding clinical characteristics, but because, together with other industrial diseases, they constitute a unique sociologic group. They represent a new alinement in medical practice and are of increasing importance because of their economic and political implications in the social class in which they predominate. Industrial dermatoses are particularly important because of the legal provisions that have been enacted in connection with them. In the development of these laws physicians are beginning to participate and should therefore be familiar with their interpretation and application, especially since such laws have become a major legislative consideration in many states and may become a federal issue. In 1937 bills on some phase of occupational disease were introduced in twenty-three state legislatures.

MEDICAL PROVISIONS

Secretary of Labor Perkins once stated (1932) that the medical aspects of the workmen's compensation laws were on the whole among the minor problems of such laws and that the chief concern and duty of the persons charged with enforcing and carrying out these laws were to see that the injured workmen received proper and adequate medical care.¹ If this implies that the compensation laws are to be so liberally interpreted that medical care is the prime requisite to be provided regardless of consideration of liability or without a strict determination of the question of liability, with the employer, the insurance carrier or the state compelled to furnish such service, there will be socialized medicine, not industrial medicine. Conversely, if medical service and compensation legally provided for a workman and applicable in his case are denied him because of some dereliction on the part of the physician, the latter is not fulfilling the social obligation which the law clothes him. Where liberal compensation laws prevail, the medical aspects are decidedly not minor problems, because their interpretation is increasingly difficult and a rigid interpretation of the medical provisions under such conditions is as much in the interest of the workman with an occupational disease as in the interest of the employer. Laxness or incompetence in medical cooperation, especially within the scope of liberal laws, will build up a tremendous economic burden for industry and can bankrupt certain

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1. Development in Workmen's Compensation Since 1930, Bureau of Medical Economics, J. A. M. A. 110:121B (Feb. 26) 1938.

industries and insurance companies and throw men out of employment. The threat of this has actually occurred as the result of the silicosis problem.

An example of the effect of liberalizing the laws may be presented from Wisconsin, which has a very capable industrial commission. As contrasted with 1920, there were in 1934 three times as many compensable cases in Wisconsin, with more than six times the expenditure for indemnity and ten times the expenditure for medical aid. In Ohio, where the laws are clearly defined and limited by schedules and where medical supervision is efficiently organized by the state department of health, there were 13,000 cases of compensable occupational disease reported in the ten year period from 1928 to 1937 inclusive, of which 67.5 per cent were cases of occupational dermatitis.² In the eight years before Ohio compensated for occupational disease (1921) there was a yearly average of 322 compensation cases; since then this average has been 1,144, or approximately four times as great.³ The manager of the conservation department of the National Bureau of Casualty and Surety Underwriters has been quoted as stating "It is no exaggeration to say that the financial life of some of our most important industries is at stake and serious effects will occur if measures are not taken to remedy the conditions causing occupational diseases."⁴ In metropolitan New York in 1936, 385 of 684 dermatitis claims, or 77 per cent, were denied by the state commission after review.⁴ Consider the economic possibilities under poorly devised "all coverage" provisions, lax law enforcement or incompetent medical supervision or service.

The workmen's compensation acts, the basis of much medicolegal controversy, have unquestionably shown a steady development toward the liberal or progressive side and a striking evolution toward national uniformity, frequently arrived at by political guidance rather than based on local and economic needs. Beginning with the Wisconsin act of 1911, providing compensation and medical care only for accidental injuries acquired in employment, compensation acts are now on the statute books of every state but two, and in twenty-eight states and five federal jurisdictions, in addition to accident provisions they now authorize compensation and medical care for occupationally acquired disease.⁵

DEFINITIONS OF INJURY AND DISEASE

To the conservative minded, the joker in the compensation laws appears to be the definition of a compensable injury. Much liberalization of the law has been accomplished by the simple expedient of changing coverage from "accidental" injury to "personal" injury and by liberally defining the latter. In the California compensation act the term injury "includes any injury or disease arising out of employment"; in Wisconsin statutes injury is "mental or physical harm to any employee caused by accident or disease"; in the United States employees' compensation act the term injury includes, "in addition to injury by accident, any disease proximately caused by the employment"; in Delaware injury or personal injury is construed to mean "violence to the physical structure of the body," while in Connecticut injury or personal injury "shall be construed to include only accidental injury which may be defi-

nately located as to the time when and the place where the accident occurred."⁵ The supreme court of Massachusetts, in reviewing a specific case, interpreted personal injury as "including any lesion or change in the human system which causes pain or incapacity for work."⁶ Either the court is too liberal in its interpretation of personal injury or that term should be excluded from the provisions of compensation laws, for the social philosophy of such provisions is paternalistic, uneconomical, unpractical and undemocratic.

There appear to be thirty states that provide compensation for some form of dermatosis. Ten states (Alabama, Arizona, Georgia, New Mexico, Maine, Maryland, Tennessee, Texas, Vermont and Wyoming) rigidly confine compensation to cases of accidental injury or personal injury due to accident in line of employment and exclude all dermatoses; eleven states (Colorado, Florida, Idaho, Iowa, Kansas, Kentucky, Nevada, Montana, Oregon, Virginia and West Virginia) recognize dermatoses only when they can be interpreted as accidental injuries, and four states (California, Massachusetts, North Dakota and Wisconsin) permit interpretation of occupational dermatoses as personal injuries and liberally define the latter. Connecticut law states that a "personal injury shall not be deemed to arise out of the employment unless causally traceable to the employment rather than through weakened resistance or lowered vitality."⁷

The clearly defined conception of a compensable injury as stated in the Connecticut law, and the restrictions placed on provisions for compensation because of occupational injury in other states referred to, appear to provide adequate protection to the workman with a legitimate claim because of an occupationally acquired injury, and at the same time they give some protection to those individuals and groups who are held legally responsible to provide compensation for such injuries. With regard to dermatoses coming under injury clauses, there is need for detailed definition. In some states it is still legally possible to obtain compensation for conditions such as lichen planus, psoriasis and syphilis when the first demonstrable evidence of such disease occurs at the site of and following an occupational or alleged occupational injury. Some physicians believe that such interpretation is justifiable, and others will agree with me that it is not and that such cases differ appreciably from, for example, cases of infectious eczematoid dermatitis and dermatitis venenata following occupational injury. Until physicians have decided among themselves the medical interpretation of such issues they cannot expect legal provision for them in the compensation laws or unified court rulings on individual cases.

What seems to have been a more logical step than distorting the definition of injury has been the enactment of provisions for occupational disease, but here also there is controversy, this time centered about the definition of "occupational disease." The Connecticut statutes (1930) define it as "a disease peculiar to the occupation in which the employee was engaged and due to causes in excess of the ordinary hazards of employment as such" and "arising out of or in the course of his employment."⁷ The general laws of Rhode Island define occupational disease as "a disease which is due to causes and conditions which are char-

2. Smith, K. D.: Report, Bureau of Occupational Disease, Division of Hygiene, Department of Health, Ohio, 1937.

3. Hayhurst, E. R.: *Indust. Med.* 6: 329 (June) 1937.

4. Sappington, C. O.: *Indust. Med.* 6: 229 (May) 1937.

5. Bull. 625, Bureau of Labor Statistics, U. S. Department of Labor, 1937.

6. Doyle, E., Massachusetts Department of Industrial Accidents: Personal communication to the author.

7. Bull. 13, State of Connecticut, 1935.

acteristic of and peculiar to a particular trade, occupation, process or employment."⁸ Michigan (1937) defined occupational disease as did Rhode Island and North Carolina and stated that the disablement of an employee by reason of an occupational disease "shall be treated as the happening of a personal injury by accident. . . ."⁹ A number of states simply name the diseases to be considered occupational or the activities in which occupational diseases may occur. These are the so-called schedules, and there are eleven states (Delaware, Michigan, Minnesota, Nebraska, New Jersey, North Carolina, Ohio, Pennsylvania, Rhode Island, West Virginia and Washington) that restrict compensation for diseases of the skin to the diseases or industries listed in such schedules. An amendment proposed for the New York law would state that "an occupational disease is a disease which is the natural and unavoidable result arising from conditions that are characteristic of or peculiar to a particular trade, process, occupation or employment in which the employee was employed or engaged."

Sappington⁴ defines an occupational disease as "one which occurs with definite frequency and regularity in occupations in which there is a specific exposure as the cause which operates to produce effects in the human body recognizable clinically by the medical profession as pathological changes and effects, produced by the specific exposure involved." The Illinois acts of 1937⁵ define occupational disease as follows:

In this act the term "occupational disease" means a disease arising out of and in the course of the employment. Ordinary diseases of life to which the general public is exposed outside of the employment shall not be compensable, except where the said diseases follow as an incident of an occupational disease as defined in this section. A disease shall be deemed to arise out of the employment only if there is apparent to the rational mind upon consideration of all the circumstances, a direct causal connection between the conditions under which the work is performed and the occupational disease, and which can be seen to have followed as a natural incident of the work as a result of the exposure occasioned by the nature of the employment and which can be fairly traced to the employment as the proximate cause, and which does not come from a hazard to which workmen would have been equally exposed outside of the employment. The disease must be incidental to the character of the business and not independent of the relation of employer and employee. The disease need not to have been foreseen or expected but after its contraction it must appear to have had its origin in a risk connected with the employment and to have flowed from that source as a rational consequence.

The Illinois definition appears to me to be the clearest, broadest and most liberal that has been introduced for occupational diseases, and it defines "blanket" or "all coverage" provisions perfectly.

PROVISIONS FOR COVERAGE

The objections raised to "blanket provisions" are that they increase the difficulties and widen the margin of error in diagnosis and that they are uneconomical. This is frequently true because of inadequacies of the law, but where blanket legislation has been intelligently interpreted and fairly applied it appears to have worked out satisfactorily, though the costs of compensation have naturally mounted considerably. A sociologic question involved is whether it is desirable to protect a workman against injury or disease only in hazardous occupations or whether it is desirable to provide for his care in any and all instances of occupationally acquired disease. The latter provision would meet a socialistic demand but would naturally increase the

financial burden, which is inevitably shouldered by the tax payer. In discussing forensic aspects of dermatitis Cox⁸ has remarked that "in the course of a year many persons suffer from dermatitis caused by external contact with some chemical substance or product of industry, those who suffer in person or through their skins, and those who suffer—not always vicariously—through their pockets, paying for the others." Are the progressive law makers giving proper consideration to this second group, and if they are not, does not protection lie in "scheduling" occupational disease and injury?

Great Britain, which compensates for incapacity for work instead of for loss of employment, has the schedule system and found that it cost £12,000,000 in 1930, with cases tripling the number anticipated when the act was established.⁹ Little emphasized the need of skilled medical inspectors in factories and constant clinical and laboratory research to reduce prohibitive costs.

Britton¹⁰ said that a fair legal plan for occupational diseases depends fundamentally on medical knowledge and that a fair knowledge of this subject is at present possessed by a comparatively limited number of physicians.

An occupational injury can usually be exactly established as to its time, place and manner of onset, but an occupational disease cannot usually be confirmed in this manner, and the history of the case, as obtained from the patient, therefore becomes a big factor in the establishment of a diagnosis. A recognition of human frailty in this regard, especially when there are monetary considerations involved, makes evident the need of more exact methods of diagnosis, or of supplementing diagnosis, than are now available in dermatologic cases in the limited fields of the not infallible patch test, the trichophyton test and laboratory aids in the diagnosis of fungous and bacterial diseases.

There are nine states (California, Connecticut, Illinois, Indiana, North Dakota, New York, Massachusetts, Missouri and Wisconsin) with blanket coverage. The International Association of Industrial Accident Boards and Commissions recommended the adoption of blanket coverage, and at a conference on labor legislation called by the Secretary of Labor in 1934 the committee on workmen's compensation recommended that the term injuries be specified to include occupational diseases and that the blanket coverage of occupational diseases be encouraged.⁵ The American Bar Association, studying occupational disease legislation in 1937, recommended the schedule system for states, with special provisions for particular diseases, and a medical board and a bureau of industrial hygiene for each state.⁴

In 1937 the legislatures of Delaware, Michigan, Nebraska, Pennsylvania, Rhode Island and Washington passed occupational disease legislation under schedule provisions, inclusive of certain specified dermatoses, such as dermatitis venenata. In 1936 and 1937 New York, Illinois and Indiana enacted blanket legislation. Oklahoma provided coverage through a state insurance law.

The Committee on Standard Practices in the Problem of Compensation of Occupational Diseases of the American Public Health Association¹¹ recommends the schedule system and includes in its list of diseases infection or inflammation of the contact surfaces of the

8. Cox, H. E.: *Med.-Leg. & Criminol. Rev.* 5: 123 (April) 1937.

9. Little, Sir E. Graham: *Indust. Med.* 7: 117 (March) 1938.

10. Britton, J. A.: *Indust. Med.* 6: 383 (June) 1937.

11. Committee on Standard Practices: *Am. J. Pub. Health* 27: 77 (supp. vol.) 1937.

skin due to cutting oils or compounds or lubricating oils, dermatitis venenata (occupations specified), epitheliomas (causes specified), ulceration of the skin due to chrome, caustics, acids and alkalis, and some other dermatologic conditions.

In schedule states the law is usually worded thus: "The following diseases shall be considered occupational diseases and compensable as such when contracted by an employee in the course of his employment and due to the nature of any process described herein." Then follows a list naming a few diseases, commonly anthrax, glanders, chrome ulcers and, more recently, silicosis, and listing oils and lubricating compounds, dusts, fumes, vapors and gases and the heavy metals. The listing of processes may be worded "any industrial process in which the use of" a specified material or "any industrial process caused" in a specified manner.

Industrial dermatoses have not been defined in any compensation law, though some schedules make provisions for occupationally acquired dermatitis venenata (Rhode Island, Michigan, Washington and Oregon). As a basis for specific dermatologic provisions in the law, it may be well to consider the hypothetical law drawn up by Sulzberger:¹²

When an employee suffers from any skin condition, or from the sequelae of any skin condition, in which his occupation can be proved, beyond reasonable doubt, to be, directly or indirectly, a causal or contributory factor, such employee is entitled to compensation commensurate with (a) the degree to which the occupation is responsible for the skin disease and/or its sequelae; and (b) the extent and duration of the skin condition and/or sequelae, the resulting discomfort, disability and/or disfigurement. Such employee is further entitled to the payment of the reasonable costs of adequate medical attention and treatment, administered through qualified physicians, hospitals, etc. of his own choice; and such employee is further entitled to such reasonable costs of investigation, and of expert testimony as may be necessary in order to substantiate his claim.

I believe this is too inclusive and have suggested modifying it to read in substance "that an employee be entitled to compensation only when his occupation can be proven, beyond reasonable doubt, to be, directly or indirectly, a causal or contributory factor in the production of the dermatosis, and that compensation be commensurate with the degree to which the occupation is responsible for the skin disease."¹³ A definition of this nature, in appropriate legal phraseology, would require provision for competent dermatologic examination. I do not consider the average employee capable of selecting competent medical aid for the examination of a special disease and therefore favor selection from a panel, but once a diagnosis of occupational disease has been established, some latitude may be allowed the employee in the matter of medical and hospital care.

CHOICE OF PHYSICIAN

Free choice of physician by the patient in compensation cases is the rule in ten states (Iowa, Missouri, Montana, North Dakota, Ohio, Oregon, Rhode Island, Texas, Pennsylvania and Washington) and is provided, with certain restrictions, by the panel system, which prevails in six or more states (Connecticut, Colorado, Kansas, Minnesota, Tennessee and Wisconsin). In eight or more states the law specifies that the employer must provide the physician. The growing provision for free choice of physician is bound to lead to participation

by a larger number of physicians in this field, and while the amount of work for dermatologists will probably increase, there will be a greater need for training of the general physician and surgeon in industrial dermatology. However liberal the law regarding the choice of physician, it should provide for the services of a specialist on the request of the patient, the employer or the insurance carrier. This applies particularly to cases of dermatosis in which there may be a reasonable question of diagnosis or a particular problem in treatment.

When a workman consults a physician privately, there is only the doctor and patient relationship to consider, but when the disease is a compensable one, or possibly so, the case extends beyond these confines and the physician should recognize the added responsibility, his limitations in the diagnosis or treatment of a special disease and his moral obligation to seek consultation or assistance when it appears indicated.

The more liberal the law, the greater the margin of error in its application and the greater the economic burden of those who pay the bill. The safeguards lie not only in the integrity of those who construct, interpret and apply such laws but also in the intelligence and honesty with which the physician carries out his responsibilities under the law. A high degree of skill in differential diagnosis and painstaking study to assemble and correlate factual evidence are necessary in many cases to do justice to both workman and employer. The dermatologist with experience in industrial dermatoses recognizes the complexities of some of these problems and appreciates the large margin of error frequently occurring when the law is in advance of average medical knowledge and skill. The law is also at times in advance of the insurance carrier, who is often unwilling to pay the initial bill for comprehensive investigation by medical experts but who patiently carries the load of prolonged dribbling compensation payments for disability and medical care in cases in which liability need never have been assumed.

COMPENSATION FOR NONDISABLING DISEASE

Sappington⁴ said "It is the intent of the laws to compensate for *disability* resulting from occupational disease; the employer should not be required to pay compensation for a diagnosis." I do not agree with this, for an untenable situation is created when the law applies only to disabling or partially disabling diseases, the workman being liable for his medical care when there is no disability, the employer when there is disability. However, this is the law in ten states (Arizona, Georgia, Montana, Kansas, Tennessee, Texas, Pennsylvania, Rhode Island, Virginia and West Virginia), while fifteen others now provide for the payment of medical care for nondisabling disease (California, Connecticut, Delaware, Idaho, Iowa, Minnesota, Missouri, Michigan, North Carolina, North Dakota, Oregon, Ohio, Massachusetts, Washington and Wisconsin). The latter provision is undoubtedly the only rational one, for it permits early examination, with resultant greater facility in diagnosis, and more effective therapy, with consequent reductions in cost. A diagnosis is the first essential step in the consideration of a potential case of occupational disease. In many dermatologic cases, in which examination by a dermatologist is not made until disability has occurred, a correct diagnosis cannot be made with absolute certainty.

12. Sulzberger, M. B.: *Am. J. Surg.* 30: 531 (Dec.) 1935.

13. Foerster, H. R.: *Observations on Industrial Dermatology*, J. A. M. A. 107: 247 (July 25) 1936.

MEDICAL BOARDS

It seems a logical procedure that laws concerning disease, the medical provisions of which were devised and enacted by nonmedical men, should be not only enforced but also interpreted by nonmedical men. I have not found legal provision in the laws of any state for the appointment of physicians as commissioners or examiners, and it is evident that in many states the weighing and sifting of medical evidence in disputed cases is done entirely without medical advice or guidance except that obtained from medical witnesses involved in specific cases. It is gratifying therefore to observe a growing recognition of the importance of physicians in this work and their assignment to it, and, no doubt, as the provisions to cover industrial dermatoses are broadened, the increasing complexities of the medicolegal aspects of dermatoses will create opportunities for properly qualified dermatologists functioning in official capacities.

At the present time the industrial commission of Ohio has on its staff a medical department of seventeen full time physicians, one of them designated medical director; the Oregon commission has six physicians, of whom one is a full time appointee, and California has five medical directors. The recent Michigan act provides for a board of three impartial physicians to investigate controversial cases, a provision that has long prevailed under Massachusetts law. Six states (Kentucky, New York, North Carolina, Pennsylvania, Washington and West Virginia) have some other form of medical board, and the commissions of six other states (Arizona, Georgia, Iowa, North Dakota, Rhode Island and Virginia) each have at least one medical adviser, usually a full time appointee. Six states (Connecticut, Maine, Missouri, Texas, Pennsylvania and Wisconsin), while having no official medical appointees, have empowered their commissions to select medical aid when it is deemed advisable.

NEW LEGISLATION

In 1935 the Maryland legislature created a commission for the study of occupational disease which conducted an investigation with the cooperation of its state health and labor departments and the surgeon general of the United States, held public hearings, and took the testimony of state and national authorities on all phases of the industrial disease question, and submitted an act for compensation legislation which was recently passed by its senate but failed of enactment in the house.¹⁴ I am reporting on it because it is a most desirable kind of legislative proposal on this subject, and if it is not subsequently enacted into Maryland law it may still serve as a model for the consideration of other states.

The proposed Maryland law provides for a medical board whose reports and findings on medical questions in cases involving occupational diseases may not be modified or changed by the industrial commission. It also provides "that in all appeals in which occupational diseases are involved, the findings of fact by the Medical Board and by the State Industrial Accident Commission shall be final and not subject to review or modification by the Court or be submitted to a jury." This law specifies that the medical board shall consist of three members, appointed for terms of six years (a new appointee every two years), two of whom shall have

had at least five years of practice in the diagnosis, treatment and care of industrial diseases and one of whom shall be especially trained in roentgenology and who shall have had at least five years of practice and experience. These licensed physicians of good professional standing shall be appointed by the governor by and with the advice and consent of the senate from a list of nominees to be submitted by the deans of the medical departments of the University of Maryland and Johns Hopkins University and by the Council of the Medical and Chirurgical Faculty of Maryland.

The 1937 Idaho legislature authorized and instructed the state division of public health to conduct a statewide survey of occupational disease and charged it with reporting on some pertinent questions.¹⁵ Information was requested on the prevalent occupational diseases, the extent of their prevalence, the best standard practices of industrial hygiene for the prevention of such diseases and what measures the legislature might promulgate to facilitate the adoption of such preventive practices. The legislators also inquired as to what measures the legislature could construct to compensate workmen disabled by occupational disease and how much compensation such workmen should reasonably receive. Also, and these questions may be unusual though important for legislators to ask, they inquired how much it was going to cost employers to insure payment of compensation for occupational diseases and to what extent the cost factor would be likely to affect the continuance and expansion of industries in which occupational diseases arise. Furthermore, they inquired as to limitations and instructions, particularly as to medical procedure and practice, to keep costs at a reasonable rate. I have reported this in detail because it is an enlightened approach to contemplated workman's compensation legislation that should receive hearty endorsement and should result in a fair and liberal law.

The Committee on Standard Practices in the Problem of Compensation of Occupational Diseases of the American Public Health Association¹¹ recommends that special provision be made in each occupational disease act for a medical advisory board to facilitate the settlement of claims, such board to be appointed by the governor from lists submitted by the state medical society. The functions of such a board would be related to the settlement of disputes regarding diagnosis, disability, causal relationship of occupation to disease and consideration of the medical aspects of claims for personal injury by accident. The members of such a board could function also as medical expert witnesses or could appoint such experts. It was suggested that qualified representatives of administrative medicine, medical economics, toxicology and legal medicine, pathology, radiology, industrial hygiene, surgery and dermatology constitute the personnel.

HEALTH DEPARTMENT BUREAUS

With exception of the health departments of Connecticut¹⁶ and Ohio,² which have long been active in this field and have accomplished much good, state health departments have not given official recognition to the subject of industrial disease until recent years. The Section on Preventive and Industrial Medicine and Public Health of the American Medical Association has long been aware of the major economic importance of

14. Waters, T. C., Maryland Commission for the Study of Occupational Diseases: Personal communication to the author.

15. Weissross, S., Department of Public Welfare, Idaho: Personal communication to the author.
16. Osborn, S. H.: Bulletin, Connecticut State Health Department, 1936.

the prevention of industrial diseases, and its activities represent the first national action of organized medicine in this regard. That section established a committee on research and standards with the object of studying and establishing standard practices and compiling information on occupational disease legislation that might be utilized by legislative and social agencies, employers, insurance carriers and labor organizations.

The entry of the federal government into the field of industrial medicine in the various states has been facilitated by provisions of the National Security Act, which has furnished funds for the setting up of bureaus of industrial hygiene within the state departments of health, which presumably will function in cooperation with the United States Public Health Service toward greater uniformity of industrial health laws and practices. Twenty-three such bureaus are now established (California, Connecticut, Illinois, Iowa, Idaho, Kansas, Maryland, Minnesota, Missouri, Mississippi, Michigan, North Carolina, South Carolina, New Hampshire, Ohio, Pennsylvania, Rhode Island, Tennessee, Texas, Vermont, West Virginia, Virginia and Wisconsin), and four are being established (Minnesota, Missouri, Idaho and Washington). Massachusetts and New York have bureaus of industrial medicine within the organization of their state departments of labor. These bureaus will concern themselves chiefly with the recognition and prevention of industrial disease, with statistical studies and with the promotion of industrial health, and they should exercise a beneficial influence on legislation. Industrial diseases are legally reportable to the boards of health in eight states and to the industrial commissions or analogous bodies in more than twelve states.

ROLE OF THE DERMATOLOGIST

One may ask "What is the place of the dermatologist in this picture?" In the states where industrial diseases are compensable and reportable, statistical studies have shown that industrial dermatoses are more numerous than all other industrial diseases together, comprising approximately 60 per cent of the cases. The dermatoses likewise frequently present diagnostic difficulties requiring the services of competent dermatologists for correct interpretation, yet dermatologists do not appear to play an important part in industrial medicine in more than a dozen states. I know of only two dermatologists functioning in an official capacity, one in the United States Public Health Service and one on the new Council on Industrial Health. None of the recent legislative enactments or proposals for medical boards operating in conjunction with industrial commissions or for industrial bureaus in health departments indicate recognition of the importance of the dermatologist in this field. An amusing commentary on this situation, which is apparently similar in England, may be quoted from the remarks of Dr. W. J. O'Donovan⁸ made before the Medico-Legal Society last year. He said in part:

When the State chooses medical referees to sit in judgment on these great problems it eschews choosing the man who is experienced in dermatology. Those who sit as judges at dog shows and flower shows are those who understand the subjects, but a medical referee advising His Majesty's representative on the Bench may be one who is singularly interested in X-rays and understands many aspects of toxicology, but has avoided any tuition in skin diseases in his youth, and has since avoided any contact with skin departments at hospitals, as they are unclean, and yet his word in regard to dermatitis goes when he is advising his Honour on the Bench, or when he passes judgment on his colleague's work.

CONCLUSIONS

While the medical provisions of many compensation laws are inadequate and ambiguous, the enlightened attitude of legislative bodies, as demonstrated in Maryland and Idaho as well as elsewhere, indicates that the door is not closed to active participation by the medical profession in the construction of appropriate laws covering industrial health and disease. Medicine, through properly selected representation, may advise in the construction and revision of medical provisions in compensation laws so that they will be intelligent, fair and impartial and may minimize the numerous controversial issues resulting when the designers of the laws have inadequate medical guidance. Similarly, medicine may participate with law in the more effective and just analysis and disposition of cases.

An achievement in medical progress in the field of industrial medicine has been the recent establishment by the American Medical Association of the Council on Industrial Health, in the development of which the industrial dermatoses committee of the Section on Dermatology and Syphilology actively participated. The title of this council is indicative of the broad scope of its sphere of activity, and one may anticipate a marked advance in coordinated medical effort and accomplishment in the various phases of industrial medicine, inclusive of medicolegal problems, through the deliberations of this body, on which the section on dermatology is represented by Dr. Earl Osborne.

To advance compensation legislation pertaining to dermatoses it will be necessary for the Section on Dermatology and Syphilology, preferably through its industrial dermatoses committee, to define properly industrial or occupational dermatoses and to establish proper criteria for diagnosis as a guide to legislative groups and with the laudable objective of reducing or eliminating controversial issues in industrial cases.

The responsibilities of this section in the medicolegal field include concerted efforts directed at obtaining enlightened legislation in every state to cover occupationally acquired dermatoses, at providing adequate instruction in the dermatologic aspects of legal medicine and at obtaining capable dermatologic representation on boards and commissions dealing with occupational dermatoses, all of which objectives may be approached through the new Council on Industrial Health.

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ABSTRACT OF DISCUSSION

ON PAPERS OF DR. LANE, DR. SCHWARTZ, DR. SULZBERGER
AND FINNERUD, DR. OSBORNE AND JORDON,
DR. DOWNING AND DR. FOERSTER

DR. CHARLES C. DENNIE, Kansas City, Mo.: This is one of the first times that such a comprehensive view of industrial dermatoses has been presented. The object of this conference is to coordinate the different factors that go into this view of industrial dermatoses and their proper handling so that justice may be rendered to the workman, to the industrialist, to the insurance carrier, and to the industrial dermatologist. Industrial dermatology is a new phase of dermatology. The industrial dermatologist must be first a dermatologist and in addition be trained especially in the recognition and treatment of industrial dermatoses. In most large industrial centers he must at least be a diplomate of the American Board of Dermatology and Syphilology. Of course that does not hold in the smaller communities. He must have on his staff an industrial nurse, technicians and possibly social service workers. The industrial nurse is a most important factor. She is more likely to pick up odds and ends that might escape the indus-

trial dermatologist and thus can make it possible for him to institute measures for the prevention and treatment of various diseases. It is important that she visit the families of workmen to determine that some factor there is not causing the dermatitis or continuation of the convalescence that otherwise would be shorter. A good illustration of that is the baker who, while he is receiving compensation, continues his same work at home in making his own bread, thus continuing his dermatitis. The next important factor is the industrial engineer, who must not only be trained in his specialty but must have a profound knowledge of sanitation in order to institute measures to prevent industrial dermatoses in industries of all kinds. The third important factor is the participation of the United States Public Health Service in this problem, for not only do these medical officers have knowledge of the different chemicals used in industries that might produce dermatoses but they know the compounds of those substances which are used in the manufacture of finished products. In the clothing industry many of these dermatoses are due to dyes the constitution of which is a secret of the manufacturer of the dyes. Officers of the United States Public Health Service also know the composition of practically all these dyes and will furnish these compositions to the industrial dermatologist, with the percentage of hazards and how they act. The fourth important thing is the medicolegal aspect of these matters. The great question is what constitutes an industrial dermatitis and what compensation the workman shall secure for it.

DR. CLEVELAND J. WHITE, Chicago: Dr. Lane's proposed graduate dermatologic instruction program would distinctly raise the professional plane of practice in occupational cutaneous diseases. A broader example of this suggestion has been the establishment of an industrial disease department in the division of medicine at the Northwestern University Medical School in Chicago under Dr. J. A. Britton. The paper of Drs. Sulzberger and Finnerud will be of immense help to all of us in trying to solve the perplexing diagnostic problems especially as concerned in the eczematous type. There is one part of this paper that I should like to comment on—the involvement of other workers in the same plant. I should like to ask how important that is. I think all of us are seeing many cases of which there is just one in that particular plant. Drs. Osborne and Jordon brought up a point that helps decide the question about the prophylaxis of cutaneous diseases and the value of the patch test. I am going to accept their opinion 100 per cent that it is of little practical importance in a large percentage of the cases when a great many tests have to be done. Osborne and Jordon's representative case of the man who had become turpentine sensitive acquiring a generalized exfoliative dermatitis brings home again the necessity of trying to determine the exact etiologic contact agent in the disease. Dr. Downing's case reports were of great benefit. There is one bit of advice by which we can all profit, and that is to give an impartial decision to the best of our knowledge, and not just make another opinion to be different. That is very important if our dermatologic advice is to be continually sought and utilized. We all endorse Dr. Foerster's suggestions so that dermatologic experience and judgment can be utilized to advance proper compensation legislation.

DR. HIRAM E. MILLER, San Francisco: In Dr. Lane's educational program I cannot understand how he expects opportunities for the study of occupational dermatoses to be found in clinics. These patients are not and should not be in clinics. They are found in the offices of the industrial surgeons and dermatologists and must be studied there. He states that insurance companies in many instances depend on the general practitioner for final diagnosis of industrial dermatoses to save expense. In this vicinity this is true only in outlying districts and in small towns. Several insurance executives have told me that they save time and money by getting the best available dermatologic opinion. I agree with Dr. Lane that medical schools should have definite courses on all phases of industrial medicine. I should like to ask Dr. Lane if in the examination of diplomats they are questioned on the subject of industrial dermatology. Dr. Schwartz states that 30 per cent of all dermatoses are found in the metal industries. I wonder whether

these figures may not be misleading. This type of industry has probably been better studied than some others. Most of the patients that I see with industrial dermatitis come from small plants or establishments with only two or three employees and absolutely no supervision as to industrial hazards. These small industries are not considered in Dr. Schwartz's figures. Some of the practical aspects of the prevention of industrial dermatoses mentioned by Drs. Osborne and Jordon will be difficult to carry out. They advise that prospective employees with ringworm should not be employed in many industries. In view of the high incidence of dermatophytosis, this does not seem to be feasible except in certain limited cases. They also state that to prevent sensitization dermatitis the patients should quit work until well and then do entirely different work. This is correct, but I do not believe that it is possible to carry it out in most instances. There are several points in Dr. Downing's paper that should be emphasized. He states that only 3 per cent of patients examined by him contested his opinion as to a nonindustrial dermatitis. It is the examining dermatologist's duty to explain to the patient why his dermatitis is not due to his employment. In most instances litigation can be avoided if this is done. It must be remembered that litigation is often of much more expense to the insurance carrier than the payment of compensation and medical care would have been in the disputed case. Another important point is that a qualified dermatologist should be a diplomat. Dr. Foerster's discussion on compensation laws is most interesting. In California the term "injury" includes "any injury or disease arising out of employment." This seems to be too broad a definition, and we are constantly forced to accept dermatoses that are very remotely due to employment. The Connecticut law states that "personal injury shall not be deemed to arise out of the employment unless causally traceable to the employment other than through weakened resistance or lowered vitality." This seems to be wisely stated and fair to all concerned.

DR. JOSEPH V. KLAUDER, Philadelphia: I may take the liberty of offering an unofficial opinion. There are many practical phases of this subject. I think it would be educational if we could hear the opinion, for example, as to this practical phase: How long should the carrier be responsible for the continuation of a chronic eczema due not to a specific agent, for example, washerwoman's eczema? Should the carrier be responsible for the further spread of the eczema? How long should the carrier be responsible for an outbreak of tinea, for example, aggravated by occupation? Should the carrier be responsible for subsequent outbreaks? I should like to call on Dr. Rothman of Budapest.

DR. STEFAN ROTHMAN, Budapest, Hungary: I thank you for the honor of being able to take part in the discussion and to hear the excellent papers. I am in charge of a dermatologic clinic at the Institute for Social Medicine of the Hungarian government. A few data concerning the industrial eczemas in Hungary may be of interest. In 1937 there were 1,500 dermatologic cases treated, 206 of which were industrial eczemas. They were all tested by a number of patch tests, the number depending on the history of the patient. Fifty-three, or about 26 per cent, of the cases were caused by crude machine oil and were seen in all kinds of workers using machines. The second large group, consisting of thirty-one patients, or about 15 per cent, was represented by workers using organic solvents for cleaning their hands, such as benzene, turpentine and acetone, or using soaps containing coal tar derivatives, formaldehyde, or turpentine and so on. Persons sensitive to turpentine are often not sensitive to the rectified product, but they are sensitive to the one used in their shop. Another group, seventeen, or 8 per cent, was that of the masons. Their sensitivity to lime, mortar or cement could not be demonstrated by the patch test as a rule but it was always suggested by the improvement which followed when the patient stopped working. Somewhat related to groups 1, 2 and 3 is group 4, consisting of thirty-nine, or 19 per cent, household workers who were exposed to very alkaline soaps and soda. Here again the sensitivity was not directly provable. The fifth group is that of the bakers, twenty-nine, or 14 per cent. Most of these were sensitive to coarse flour containing some bran and not to fine flour. None of them were sensitive to substances used as baking powder or

for bleaching. Seven cases of occupational primrose eczema were also observed. Three patients were gardeners, but four were waiters in a big hotel where the primrose is favored, as it is in spite of frequent warnings in many places on the continent. A case of sensitiveness to fly poison extensively used on farms is noteworthy. Another interesting case, which was observed several years ago, is that of an employee of a street car company who had continuously handled coins during his daily work. He had a severe exudative eczema on the uncovered parts of the body before the sensitivity to nickel and copper was discovered by testing with solutions of nickel and copper sulfate in a dilution of 1:10,000. The remainder of cases were caused by mechanical and thermic trauma. This is a small group of cases but is representative of the material that is seen every year. In questions of compensation and change of occupation we have, as I have noted, the same difficulties as you have in this country.

DR. R. H. BLAISDELL, Boston: It would be useful in the larger communities if the insurance companies could establish a central agency to which cases of reemployment could be referred. For instance, recently I saw a dissolver who received a dermatitis from sodium silicate. I recommended that he be given a different form of employment. He was given an outdoor job under a foreman in the yard, but in the course of his work he cleaned out freight cars which still contained sodium silicate and he had a recurrence. Protection is excellent, but protection itself has its hazards. A tannery that had trouble provided its men with rubber boots, rubber gloves and rubber aprons, but the men were permitted to work with bare arms from the tops of the rubber gloves to their shoulders, and the net result was nothing. A division of a chemical plant was having trouble and gave its workers rubber gloves. The first shipment consisted of yellow rubber gloves, and the resulting dermatitis was more expensive than the original outbreak from the chemicals. The dermatologist has a distinct place in the medicolegal phase. In Massachusetts in 1935 a new section of the law was added whereby all cases of industrial disease shall be referred to a board of impartial referees. The cost of such a referee examination was \$15 for each of three men, \$45 for each examination, and where there were hundreds of cases the expense was intolerable. The net result was that the Industrial Accident Board made a ruling that industrial dermatoses are industrial injuries and not diseases. The act also provided that the conclusions of this impartial board should be final by diagnosis only and not with any judgment as to industrial complications. Therefore the cases come before the referee board and return to the industrial board with a diagnosis of dermatitis and it is left to the industrial board, the layman, to determine whether that is related to the work or not, and when the workman turns up before the referee board having completed his examination they return the illuminating diagnosis of no disease, and in several cases the workmen received no compensation at all; then the board wisely made a change providing that the referee board's finding should be final as of that day only, and that their own findings should depend on the previous testimony and future testimony. If I may take the liberty, I should like to add to Dr. Dennie's list one thing, that is, the plain, everyday, ordinary taxpayer, who in the long run pays for all this.

DR. H. J. PARKHURST, Toledo, Ohio: It is very well to advise that the patient be given a different job, but this advice may have no practical value. The employer's hands are often tied by seniority rules, so that he is unable to place the patient in another occupation in the same plant, even in his own plant. The patient is often too old to find suitable work elsewhere so as to support his family. He may have spent years acquiring skill at a certain trade and be unable to change his work and still support himself and his family. He should not then become a public charge; that would be wrong. It is up to us to improve our preventive methods, especially regarding ointments, pastes and similar protective applications. There are certain applications of this kind on the market at present, but they are far from being infallible.

DR. ELMORE B. TAUBER, Cincinnati: I want to suggest that these papers be published as a monograph.

DR. M. T.-R. MAYNARD, San José, Calif.: I think the patch test has been somewhat slighted in the discussion today, and I want to make a few remarks appropos of that. First, the application of the patch test should be made as close as possible to the area that is reacting, if possible even within the border of that area. If no reaction occurs at the time the dermatitis is active, it is also advisable to repeat the patch test after the dermatitis has healed, because then one may get a positive reaction when the patient has not used up his antigens. Secondly, is it possible to reproduce the conditions under which the patient works? I recently had a case in which a man was reacting sharply to the leather dye in the tongues of his shoes. He failed to produce any positive patch test to the tongues of his shoes, but he had been working at cleaning out kilns in a pottery factory, and he would go into these kilns when they were quite hot, and his feet would sweat profusely. When sent back to work with a patch test in place he reacted to it markedly. Another thing is the dilution of the irritant. Naturally if a man is exposed to hydrochloric acid or sulfuric acid or some strong irritant he will react to that. One has to use dilutions that are tolerated by the skin without a lytic action but which will produce an allergic response. The reaction should be read immediately on removal but should be read again probably within five days and even sometimes within two weeks, because a true allergic response will often not occur on the immediate removal of the test but will show up later. I had one reaction that developed almost two weeks after the application of oil cloth, and it persisted for three weeks thereafter exactly in the configuration of the patch test. A word of caution: Do not run the risk if the patient is highly allergic of applying very much of the substance to which one suspects that he reacts, otherwise he may develop a generalized exfoliative dermatitis or exfoliating reaction. These remarks are hardly necessary for the dermatologist, but I assume that there are many here who are not dermatologists.

DR. JOSEPH GRINDON, St. Louis: A point already mentioned by Drs. Osborne and Jordon and repeated by Dr. Miller is the importance of the cleansing agents used after the day's work is finished, such as strong soaps, among others soaps containing cresol or mercuric iodide. All medicated soaps, all soaps advertised as "health soaps," all soaps advertised as being endorsed by the medical profession, are anathema maranatha. The only thing that should go into soap is soap. Another thing to deplore is the aggravation of industrial conditions by unwise therapy. Some cases are made worse by the use of ammoniated mercury. The U. S. Pharmacopeia lists an ammoniated mercury ointment of 10 per cent strength, whereas 2 per cent is plenty, usually. One other thing: Almost every general practitioner, when he prescribes an antipruritic lotion, uses phenol. The common zinc calamine lotion, pink lotion, will have some phenol in it. I never use phenol. Of course it is an antipruritic, but a large minority of the population are atopic to phenol, so that I think it wise to leave it out altogether, especially as there are other antipruritics that are just as efficient, such as resorcinol.

DR. E. F. TAUB, New York: In New York State only within the last two or three years have the dermatologists been given any recognition at all on the Committee on Industrial Diseases, and then only on a subcommittee. The problems that have come up before that committee have probably been largely of local interest, but I should like to mention two or three that have caused us the most trouble. One is the matter of pay for the physicians who examine and study a case and then that case proves to be in their opinion not of industrial causation; the insurance carrier will not infrequently refuse to pay the doctor for the examination and the time spent in making a diagnosis. Probably this causes many a physician in cases in which there might be the slightest doubt to place the case in an industrial category simply because he knows that only in that way is he sure to be paid. There should be some definite provision for payment in these cases. Another point that has caused difficulty is the matter of cutaneous testing, particularly the trichophyton and patch tests. We have recommended that the trichophyton test be given no consideration whatever as a diagnostic agent. In most cases the trichophyton test if positive does not signify that that particular eruption is ringworm in any sense, nor does a negative

test exclude ringworm; hence the test in any single given case is of no value diagnostically. Patch tests as performed rarely duplicate the patient's actual working conditions. In the first place we are often not supplied with all the materials he actually handles and if we test him with other supposedly similar chemicals they may actually not be the same, as they have come from another manufacturer, who may have used an entirely different refining process. If we are given the exact materials we do not always find it easy to simulate the exact conditions of employment in which friction, trifling trauma and other conditions may play an important role. Therefore it should be emphasized that a negative patch test would not necessarily exclude the case as an industrial one and a positive patch test might not necessarily prove it, as the testing may not have made due allowance for possible primary irritants.

DR. C. GUY LANE, Boston: Both the theoretical side and the practical side have been well emphasized today by the papers in this symposium. The three most important items which are necessary at the present time have also been emphasized. It is difficult to place these in logical order. As I mentioned earlier, education is a prime necessity. I think also that the matter of definition of criteria is perhaps of equal importance, definition of criteria in general, definition of criteria as outlined by Drs. Sulzberger and Finnerud with regard to dermatitis in particular, and with regard to termination of disability. The matter of definition of terms used is important, and I believe that the Council on Industrial Health can help out a great deal in these particular phases. The third item of importance is the matter of investigation. The investigation of causes, as brought out in Dr. Schwartz's paper, and with reference to prevention by Drs. Osborne and Jordon, are two of the prime needs in this particular field today.

DR. LOUIS SCHWARTZ, New York: I want first to answer Dr. Miller, who questioned the figures that I quoted as to causes of dermatoses in the United States. The figures from which my charts were compiled were gathered from states which have laws reporting occupational dermatoses. Those states send monthly, some of them weekly, reports to my office of the number of cases of occupational dermatoses, the causes and the industries in which they have occurred; the tables were compiled from those figures. They comprise over 9,000 cases that have been reported to my office. The remarkable thing about them is that our statistics correspond closely to similar statistics compiled in England, and from what Dr. Rothman said they correspond closely to figures compiled in Hungary. One of the doctors in his paper stated that he believes in removing from the job all workers who contract dermatitis. In my experience in factories I have found that there are many new workers who come on a job where there is a skin hazard who contract a dermatitis, but if they stay on the job for a while, a week, two weeks, three weeks, with this mild case of dermatitis, they are apt to become immune or, as the workers say, "hardened to it." If you take such a man off the job and let him get well, he again develops a dermatitis if he goes back to the job again; but if you let him continue on the job and let him get well on the job, giving him protective clothing, ointments, and what-not, while he is working he is apt to stay immune as long as he is working, and this immunity will last perhaps a month. If he discontinues work, he will retain his immunity for a considerable length of time, say two or three weeks or a month, but if he leaves that occupation for six months or a year and returns again he is apt to go through the dermatitis and hardening process again. Old workers who work at a job can pursue it for as long as twenty years without any trouble and then develop dermatitis at the end of that time; they have developed a sensitivity to some of the chemicals with which they work. Such workers never develop an immunity and they should be taken off the job and given another occupation where they do not come in contact with the irritant to which they are susceptible. Dermatologists who are called on to diagnose industrial dermatoses and to testify before industrial commissions should familiarize themselves with the exact nature of the patient's work. It is not sufficient for them to look at the lesion and do patch tests and give testimony and expert opinion on that.

DR. CLARK W. FINNERUD, Chicago: It is the opinion of Dr. Sulzberger and myself that so far as is practical it should be stressed that, although the physician should be familiar with the laws at least in his own state, he should confine his opinion purely to the medical aspect of a given case. The legal status has appeared to us to be solely the function of the legal profession, although, as mentioned by Dr. Foerster, medical criteria must be plainly formulated for the legal profession by the dermatologist. We have tried to incorporate in the paper essential definitions throughout. In answer to Dr. White, if I understand his question, I would say that the presence of a similar disorder in other workers in a given plant simply adds weight to the physician's opinion as rendered in a given case. We appreciate the shortcomings of our tables of criteria, but the text in a measure clarifies some of these points.

DR. EARL D. OSBORNE, Buffalo: Dr. Miller referred to the statement which Dr. Jordon and I made regarding the presence of ringworm as a reason for turning down a worker for employment. We referred, of course, only to the presence of a generalized sensitivity, or dermatophytid, in the presence of an active ringworm, and not to a localized chronic ringworm of the toes, as a reason for refusing employment. Regarding the point that Dr. Schwartz mentioned, namely, the hardening process, I am of the opinion that it does not apply to sensitization dermatitis. That has been demonstrated clinically and experimentally as not occurring. It has been shown that, once a person has developed a sensitization dermatitis to a certain specific chemical, it requires many days, months or years for that dermatitis to disappear, and sometimes it never does. My impression of the hardening process is that it occurs when individuals are exposed to a primary irritant repeatedly over a number of days, resulting in a hyperkeratosis which acts as a mechanical protective agent. I want to emphasize again that experimentally, scientifically and clinically there is no such thing as a hardening process in true sensitization dermatitis.

In mentioning the transfer of an employee from a job to some other type of job, we referred only to individuals who had developed a sensitization dermatitis and not to individuals who had a primary irritative dermatitis. I believe that one of the most important things in the prevention of industrial dermatitis due to sensitization is the early recognition that it is a sensitization dermatitis and not an irritative dermatitis, with the transfer of that employee to another job where he does not handle the offending allergen. In New York state we have a rehabilitation committee assigned to each industrial board, and every employee who develops a true sensitization dermatitis, where we recommend that he be transferred to another job, has his case taken into consideration by this committee and he is placed in some other line of employment, or the plant or industry finds other work for him. We do not refer to the application of patch tests in the diagnosis of industrial dermatitis, only to the preemployment examination. My own impression of patch tests as applied to diagnosis is the same as in the practice of dermatology generally—only a well trained dermatologist with a great deal of clinical experience in evaluating the application and limitations of the patch test in practice should do it. In my opinion, clinical trial and experience many times are of greater value than the patch test in industrial dermatoses.

DR. JOHN G. DOWNING, Boston: At our exhibit on industrial dermatoses, various observers cited interesting cases of ergodermatoses occurring in their practice. Physicians should report these cases, for such reports may help to solve the problems of other medical men. For example, a clinical note on dermatitis due to sawdust (Levin, O. L.: Sawdust Dermatitis, *THE JOURNAL*, Feb. 25, 1933, p. 570) helped to solve the question of an outbreak of dermatitis occurring among building cleaners who were in contact with numerous irritants at their work. Patch tests with the sawdust with which they came in contact were positive. The workers were supplied with a small shovel with which to scatter the sawdust about, and no more cases occurred until a year later, when a shovel broke and was not replaced and a new outbreak occurred. I agree with Dr. Schwartz that it is better to keep a man on the job, for he may become desensitized and is less apt to get a compensation complex.

All dermatologists have seen workers, such as molders of bakelite, who have been able to work for years with only periodic attacks of dermatitis which have been relieved by treatment while the patient continued to work. These men, however, should be watched carefully; they should be examined daily, and if their eruptions continue to spread to any marked extent they should immediately stop work. As long as the eruptions remain stationary or improve there is no reason for the patients to stop work, because if these men stop work they rarely can return to their trade.

DR. HARRY R. FOERSTER, Milwaukee: I cannot agree with the suggestion that legal considerations be left to the legal profession; there is too much involved in this question of medicolegal interpretation of industrial dermatoses. Controversy arises chiefly in states that have "blanket coverage," such as progressive Wisconsin and liberal California, referred to by Dr. Miller. Wisconsin was the first state to have a compensation law and the first state to appoint an industrial commission. Originally coverage applied only to injuries sustained in occupational accidents, and that law is still on the books, but injury has been redefined, so that injury is now interpreted as "mental or physical harm" to an employee. That may mean almost anything. The only safeguard to the employer in a state with such liberal laws lies in an efficient commission. While in our state the examiners and commissioners are laymen, fortunately they are intelligent, capable and experienced and they exercise a good deal of judgment and common sense in their interpretation of cases.

ALLERGY IN CHILDHOOD

PROPHYLAXIS, EARLY RECOGNITION AND TREATMENT

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Any attempt to reduce the incidence or severity of a prevalent disorder is certainly worth while. And certainly the axiom "an ounce of prevention is worth a pound of cure" is a most practical one, especially as it pertains to childhood allergy. The management of allergic children might be said to begin with conception.

Research by several investigators, most noticeably Ratner, reveals the possibility of active or passive intra-uterine sensitivity. Observance of mothers from conception to delivery presents certain ideas which apparently have practical significance. Sensitivity of the skin to foods such as eggs which have not been ingested or with which an infant has not been in contact suggest inherited or intra-uterine sensitivity.

It is a frequent observation that clinical sensitivity often abates during pregnancy. Such knowledge plus the possibility of passing specific sensitivity in some manner to an offspring should make mothers reasonably avoid during pregnancy the foods to which previously they were clinically sensitive. Moreover, as an overindulgence of any food is more apt to result in sensitivity than when moderate amounts are ingested at intervals, food cravings should not be indulged during pregnancy.

Since milk, especially the lactalbumin, and eggs are the foremost etiologic allergens in infancy, it seems reasonable to suggest that mothers drink boiled milk in the later months of pregnancy and avoid an excess of eggs. It is also plausible not to force foods to which there is a definite and prolonged dislike.

Before the infant of allergic parents arrives, its future environment, especially its room, should be prepared as free from inhalant substances as possible. While it is admitted that the majority of allergic disorders of infancy are traced to foods, inhalants such as feathers, hairs, face powders, sprays, kapok, dusts and pollens are not infrequently etiologic factors.

The next prophylactic measure is concerned with the new infant's diet. People have been brought up to believe that milk is the most perfect food for every one, little or no allowance being made for those with lactalbumin or casein sensitivity. Fortunately the use of boiled, powdered or evaporated milk usually takes care of sensitivity to the lactalbumin factor. While undoubtedly the majority of infants take some form of milk well and thrive nicely, more than is generally agreed on cannot tolerate it clinically. When casein sensitivity is present boiling, powdering or evaporation of milk, contrary to statements or propaganda in favor of evaporated milk, does not overcome the trouble. Owing to the increased permeability of the intestinal mucosa during the first two or three days of life, it is wise not to offer cow's milk then. The use of "vegetable milks" is generally very satisfactory when casein sensitivity occurs and in my experience is most satisfactory to patient, parents and physician. There appears to be no increase in sensitivity from the use of "vegetable milks"; on the contrary, when the main allergic factor is milk, the forcing of it in a casein-sensitive infant is likely to give rise to further food trouble.

When a new vitamin substance or food is introduced a small quantity should be offered once and not repeated again for three days. Such an interval gives ample time for sensitivity to manifest itself. Among potentially allergic infants it is better to introduce a single substance and avoid mixed cereals, fish oils and vegetable soups the contents of which are composed of many items. Apparently foods consistently disliked or regurgitated should be avoided and the diet varied. Too early introduction of vegetables and fruits, some feel, is apt to encourage allergic disorders.

Signs and symptoms suggestive of an allergic disturbance are recurrence of head colds, itching, sneezing, coughing, wheezing, hoarseness, croup, abdominal pain, eczema, hives, excessive regurgitation, constant discomfort, excessive constipation, mucus in the stools or loose stools and sudden swelling. Respiratory disorders which are not contracted by others in the family suggests an allergic background.

In the treatment of allergic disorders, not the allergic condition alone, such as eczema, needs treatment but the infant with eczema. While symptomatic or palliative remedies are of some value, it is to be remembered that the disorder is probably due to some substances ingested or inhaled, and proper care must be exercised to minimize future sensitivity.

To avoid or at least to reduce the incidence of reactions from immunologic procedures, they should be given early and when the child is approximately 1 year of age the following procedures should have been completed: pertussis vaccine, diphtheria and tetanus toxoid, Schick test and vaccination. Such a course reduces the need of subsequent serums, which in allergic infants are not without potential danger.

After the patient reaches childhood it is much more difficult to find the etiologic factors. A more detailed investigation is necessary and more reliance has to be

placed on dermal and intradermal tests than is necessary in infancy. In addition to the signs and symptoms already mentioned, frequent sniffing, nasal itching, headaches, fatigue, eructation, "canker sores," fever blisters, colitis, circumoral pallor, subocular discolorations or edema, so-called sinus infections, night sweats and the like are found. In cases in which there is a persistent dislike for certain foods (especially if parents are not finicky and table manners are pleasant) or a craving for some foods, some information is available which at times proves to be of clinical value.

On physical examination the allergic child often shows pale, waterlogged inferior turbinates, overbite or teeth irregularities, a prominent nose, pinpoint papular lesions of the conjunctivae or small areas of excessive lymphoid tissue in the pharynx. He is frequently seen rubbing his nose to relieve itching, the so-called allergic salute. The child may be of the overactive type and appear fatigued occasionally and his span of attention may be short.

A comparative value of cutaneous and intracutaneous tests in the same hands will usually reveal vast superiority of the latter tests. Intracutaneous tests had best be preceded by cutaneous tests to avoid the possibility of unpleasant reactions. No set standard should be used for judging positive tests—each subject requires a somewhat different standard. Positive tests may reveal past, present or future sensitivity. They should be correlated etiologically by clinical history or vice versa. Avoidance of all definite positive foods or inhalants (so far as is possible and practicable) should be attempted; then after an interval of from six to twelve months, single foods should be reintroduced at the rate of one at intervals of three days. In such manner very few of the foods eliminated are still likely to give rise to clinical allergic disorders.

The exact number of allergens to be used for skin tests can hardly be foretold; approximately from 100 to 150 is the optimum amount. A large assortment should be utilized as is consistent with the age and cooperation of the patient in question plus influences such as environment, seasonal variation of symptoms and foods generally consumed by him. At times it is advisable as well as valuable to retest patients, especially when clinical results are not as good as desired. There is no accord as to how extracts are to be prepared or standardized; hence results are apt to vary even more so than is usual in medical circles. Since it takes a period ranging from days to several weeks to eliminate completely foods causing clinical allergy, elimination diets, I feel, are of limited value. Such diets are of more value when a complete allergic study is impossible or impracticable or after a thorough investigation has been of no value.

At times direct testing of the skin is impossible or impracticable; in such instances, approximately as good results may be obtained by passive transfer tests. The usual indications for such a procedure are when there is lack of cooperation, when it is difficult to do intracutaneous tests on infants or very young children, among those who have a generalized eczema or more or less constant urticaria, asthma or angioneurotic edema, and in those who have a marked dermatographia.

Whereas avoidance might be preferable for clinical sensitivity to inhalants, such is not often possible or practicable, and specific antigens had best be given in an attempt to obtain a tolerance to those substances.

Leukopenic indexes are of questionable value among children, in whom there is normally a wide variation of the leukocyte count. The procedure is too slow and is painful to little children, and it is difficult to keep children quiet for an hour. The test is subject to too much personal error and is time consuming. The arbitrary standard of selecting a drop of 1,000 cells as significant of sensitivity is, at the best, open to question. It is obvious that a drop of 1,000 cells in a fasting count of 4,000 white cells is more significant than when the fasting count is 12,000 white cells. Moreover, if a food which previously has given trouble has been avoided for months, the reintroduction of it, if it is still a major cause of trouble, is apt to send the white count lower than when that food had been continuously eaten. When clinical observation and skin tests are misleading, leukopenic indexes apparently have their greatest place.

Removal of tonsils and adenoids for relief of allergic disorders will generally meet with failure. Likewise, surgical nasal procedures had best be avoided. Ionization of the nasal mucosa, frequent nasal packing or roentgen therapy of the sinuses is of little value in allergic rhinitis or sinusitis, as such treatment is directed to the result and not to the cause. Proper allergic care usually reduces the engorgement of the nasal mucosa, permits physiologic drainage and gives more breathing space. When tonsils and adenoids are to be removed, that procedure should be attempted during the season in which pollens are not prevalent, to avoid a subsequent pollen hay fever or asthma, which far too frequently seems to follow. Smears of the mucus or mucopurulent nasal drainage among allergic children usually show an eosinophilia. Such a finding per se should put one on one's guard when nasal procedures are contemplated.

Instructions to parents should be in writing to avoid misunderstanding. Foods apt to contain forbidden articles should be mentioned. Recipes are often needed when milk, egg and wheat sensitivity exists.

Transfusion among allergic children is not without some potential danger. Careful inquiry should be made into the donor's possible allergic background, and his blood should be taken just before a meal, if time permits. This reduces reactions to the donor's blood resulting from reagins in the donor's blood to which the recipient is clinically sensitive. Intradermal tests with the donor's blood is an added precaution.

When it is possible to modify the severity of a disease, as with measles, or possibly to immunize against one, as with pertussis, it should be considered, as those diseases are too frequently followed by asthma. Vaccination should be deferred among infants and children with eczema, as there is danger of a generalized vaccine due to dissemination of the virus through the blood to the eczematous areas of the skin. Untreated eczema of infancy is apt to turn into asthma or recurrent bronchitis of childhood. Such is unfortunately often true of croup of infancy. Gastrointestinal upsets of infancy may become paroxysmal headaches or migraine later. Uncorrected recurrent allergic rhinitis at times becomes hay fever or asthma in later years. When there is definite or suspicious sensitivity to horse serum, serum of another animal should be used if possible.

No matter what the nature of the allergic disorder, one should not forget the importance of good health and habits. The allergic balance is apt to be better maintained when the physical and mental condition is good.

CONCLUSION

The care of allergic children begins in utero. In view of the frequency of abatement of clinically allergic symptoms during pregnancy, mothers should be warned to abstain from or eat cautiously foods they know have previously given trouble. They should also be warned not to satisfy food cravings. Before the arrival of the infant its room should be clean and free from inhalant substances such as hairs, feathers and dust. Early allergic symptoms should be sought and mothers taught what to expect, and when the cause is found it should be eliminated. Preventive measures given early reduce reactions and need of subsequent serums. After a child becomes several years of age, it is more difficult to find the etiologic allergic factors. A detailed search by means of exhaustive history, scratch tests and the use of intradermal tests enable one generally to find the cause. Intradermal tests are far superior to scratch tests. By elimination and diet correction and at times through specific antigen reactions, it is usually possible to hyposensitize or completely relieve allergic disorders in childhood and probably reduce the incidence and severity of allergic disorders of adult life.

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ABSTRACT OF DISCUSSION

DR. GEORGE PINESS, Los Angeles: I question our ability to choose foods because of their being less potential possibilities as sensitizers; therefore I would suggest the following in the handling of the potentially allergic or allergic child from a dietary standpoint: I do not think doctors, or the parents of the children, are sufficiently alert or so food wise that they can determine which foods are less potential sensitizers. Therefore I suggest that the diet for the infant be diversified, that smaller quantities of a particular food be administered, with greater variety to choose from, and that the interval between the repetition of a suspected food be greater. As Dr. McGee suggested, a three-day interval between certain foods is perhaps a good one, although from practical experiments I am convinced that the greater the interval between successive feedings of the same food the better and the less possibility there will be of acquiring sensitivity to it. I would suggest that foods such as pabulum, which contains fourteen or fifteen ingredients, be avoided as long as possible and that the food combinations used be simple and of single content if possible. In making a survey recently of about 1,000 histories at the Childrens Hospital, Los Angeles, I was surprised to find that my impressions of certain foods were erroneous in that those I suspected as being most frequent offenders proved to be otherwise. It is the general opinion of most pediatricians and allergists that wheat is perhaps the commonest offender. In the group mentioned it was fifty-fifth on the list. The most common food to give both clinical symptoms and cutaneous reactions was tomato. The most common cereal was barley. It gives one considerable to think about when one figures that elimination diets eliminate the foods that are thought to be common offenders and on specific evidence prove not to be. Foods and foods alone are not the commonest cause of allergy. It is just as common to find that inhalants and environmental allergens may cause any of the allergic conditions that were observed. Rowe in his paper yesterday discussing food allergy as a cause of bronchial asthma proved on his own charts that 40 per cent of his patients are sensitive to pollen and over 40 per cent to environmental proteins and that the general rule of multiple sensitivity acceptable to all of us occurred in his group as well. I want to emphasize the suggestions made by Dr. McGee concerning surgical procedures for the relief or alleviation of allergic symptoms. On the other hand one must not neglect to remove any pathologic condition that can be removed by surgical means, but the assumption that it will cure allergy is not justified. Dr. McGee expressed

without doubt the opinion of most workers that the leukopenic index has little if any value from a practical or experimental standpoint in the field of allergy. This is confirmed in recent articles of Lovelass, Brown and others.

DR. MARGARET M. NICHOLSON, Washington, D. C.: The point to bring out is that we happen to be treating an allergic child and not caring for the allergic state. A child may have cutaneous sensitiveness to certain factors and yet not be sensitive to them clinically. In Washington, the child of a man who is a food faddist was sensitive to carrots. Neither the father nor the mother nor the child had ever tasted carrots or any derivative of carrots. The child was taken out of the home and psychologically adjusted and never again had asthma. Depriving a child of foods essential to normal growth and development in pursuance of a theory prevalent at the time may damage him for life. I emphasize the point Dr. McGee brought out about the three days elapsing in the intervals between eating each new food by giving the mother a chart and she checks every new food, allowing three days before she repeats that food, and then repeats it three times at three day intervals. As to the vitamins, my eczematous patients have improved remarkably on very large doses of vitamin B. Of course, it may be that they have been on such rigid diets because they were sensitive to certain substances that they were markedly deficient in vitamin B at the time I obtained them. It is well known that among Negro families in the South certain children can eat tomatoes if they are picked from the vine but that if the tomatoes are allowed to stand a day or two before they are eaten, the children will have a rash or asthma. Recently at a meeting in Boston it was brought out that this has a great effect on the vitamin content, so I was wondering whether the old theory probably had truth in it. Concerning the endocrines, it seems that frequently I have seen exhibits of children who were endocrinologically affected following asthma, I think probably the result of the vitamin deficiency. The psychologic upset that these children have following any allergic state is one of the main factors. It makes them annoying citizens in later life because allergic children are spoiled and quite a problem in all the schools.

DR. JULIAN COHN, Los Angeles: I find in the practice of allergy that among the profession generally and in some cases among the pediatricians particularly the diagnosis of allergic states seems to go begging. I find that the inherited factors are not given much consideration. This is particularly true in cases of undiagnosed cough. Some parents, when asked specifically, prove to have some type of allergy, if it isn't any more than a nasal block or postnasal drip. Many parents who assert freedom from any allergy in the family, on being questioned more thoroughly, will acknowledge some form of allergy in the family. Their inherited traits will show that many of the parents and possibly the relatives eventually will acquire asthma, a wheezing particularly. It is also true that many of these children, with cutaneous manifestations in the flexure regions and around the neck, will acquire asthma some time later. I find that the scratch reaction isn't worth anything. My condemnation is not to be taken that it should be eliminated, but one should remember that the scratch test gives positive reactions in possibly no more than 25 or 30 per cent of cases while the intracutaneous method gives positive reactions in from 65 to 75 per cent of all cases. In some cases there is a lack of cooperation on the part of the parent. The parent is the greater problem permitting the patient to eat anything he desires. I agree with Dr. Piness on the interval allowed between additions of new foods. I usually insist on from seven to ten days before adding others.

DR. W. AMBROSE MCGEE, Richmond, Va.: With regard to the interval of three days, I believe that a number of pediatricians observe no interval at all. They start one food right after another, and especially is that true of vegetable soup, with which so many of them begin. I should have said that an interval of three days would be a minimal interval and that a longer one would be preferable. I also agree that inhalants are a much greater cause of trouble than has been thought in the past; even such conditions as eczema might be

due largely to inhalants, and to simply treat the food factor without the environmental factors would not produce results. An inhalant will cause just as much trouble as food and cause the same type of symptom as a food. I agree with Dr. Piness's list of foods that he has found in a study of 1,000 children. I think most of those are children of 2 and above. When I mentioned milk and egg as one of the main factors, I had reference to infants usually under 1 year of age. Cutaneous tests are not infallible but they give a working basis to start from. Skin tests do not determine whether one is allergic. Let me stress that again. It is the history. Egg yolk is not nearly so common a factor as egg white, but one does find egg yolk sensitive patients. When one has children on those rigid diets it is necessary to care for vitamins and minerals in the new diet. As to personality changes, one sees children who are spoiled and present other behavior problems clear up beautifully after one gets them straightened out from an allergic standpoint. I believe that nasal allergy is frequently overlooked and is usually referred to as the so-called postnasal drip or nervous cough. If the allergy is corrected, the cough usually disappears. I also agree that scratch tests are more or less worthless in comparison with the intracutaneous ones. Those who try to rely on results from scratch tests alone are going to keep patients from going to some one who really will study them completely. In reference to our chairman's comment about water, I think he is right and I would also like to add that since we get so much of our information from the animal kingdom, and animals do not seem to take milk after infancy, are we right in advocating a quart of milk daily for every child, provided, of course, minerals, vitamin and other needs are satisfied through other sources?

Clinical Notes, Suggestions and
New Instruments

ARTIFICIAL CONCENTRATION OF TEST SERUMS
IN BLOOD GROUPING

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The advantages in speed and accuracy of the combined Vincent-Coca technic for the grouping and direct matching of blood prior to transfusion have been emphasized in a recent report from the Cincinnati General Hospital.¹ Since the adoption of this method as a routine we have relied successfully on one minute macroscopic grouping in more than 3,000 consecutive blood transfusions. However, the serums used during this time have excelled the requirements of Coca's grade I² (table 1).

The safety of rapid open macroscopic grouping depends entirely on the use of test serums of extremely high hemagglutinin titer. Donors whose serum meets these standards are rare, and finding them is accomplished only after considerable search.

Consequently a method for concentrating the hemagglutinins in serum is highly desirable. Artificial concentration by alternate freezing and thawing has been proposed by Terry.³ The lyophile method of drying serum as reported by Flosdorf and Mudd⁴ appeared to us as a possible method for accomplishing the same purpose. We have been able to dry serum by this method and redissolve the residue in less than the original volume. The resulting product was found to have a hemagglutinin titer greater than the unprocessed serum and to be suitable for use as test serum.

Dr. Mahoney is Fellow of the National Research Council.
From the Department of Surgery of the College of Medicine of the University of Cincinnati and the Cincinnati General Hospital.
1. Hoxworth, Paul, and Ames, Axel: Blood Grouping and Compatibility, J. A. M. A. 108: 1234 (April 10) 1937.
2. Coca, A. F.: A Slide Method of Titrating Blood Grouping Sera, J. Lab. & Clin. Med. 16: 405 (Jan.) 1931. Hoxworth.
3. Terry, M. C.: High-Titer Blood Grouping Serum, Proc. Soc. Exper. Biol. & Med. 33: 14 (Oct.) 1935.
4. Flosdorf, E. W., and Mudd, Stuart: Procedure and Apparatus for Preservation in "Lyophile" Form of Serum and Other Biological Substances, J. Immunol. 29: 389 (Nov.) 1935.

TECHNIC

Under sterile precautions 200 cc. of anti-B serum was dried by the lyophile method. The solid was then completely dissolved in 50 cc. of sterile distilled water and the solution was found to contain active anti-B hemagglutinins when placed with known sensitive anti cells. Samples of the unprocessed and processed plasma were then compared for anti-B hemagglutinin potency according to the method of slide titration described by Coca.² The results of the titrations are given.

DATA

Serum which would agglutinate macroscopically an equal volume of anti cells in whole blood in twenty seconds was processed, resulting in a serum which under the same condi-

TABLE 1.—Comparison of Agglutinin Titer of Serums Used at Cincinnati General Hospital with Grade I (Coca) Serum

Serum	Serum Dilution	Cell Dilution	Macroscopic Agglutination Time
Grade I (Coca).....	1-4	1-4	11 seconds
Serum at Cincinnati.....	Anti-A 1-10	1-4	3 seconds
General Hospital.....	Anti-B 1-10	1-4	5 seconds

tions agglutinated the same cells in four seconds (table 2). This indicates that the hemagglutinin titer of the serum was increased in inverse proportion to the volume. The processed serum was then rediluted to the original volume and the hemagglutinin potency was the same as that of the unprocessed serum. Similar results were obtained with this serum in various dilutions and with other serums, both as to retention of group specificity and as to the concentration of agglutinins. In most instances it was possible to obtain, within two minutes, complete solution of the dried product in one fifth of the original volume of the serum. Imperfect drying resulted in a gummy product which resisted solution, and the hemagglutinin activity of the supernatant liquid was markedly lowered or absent.

SUMMARY AND CONCLUSIONS

Rapid macroscopic methods for the grouping of blood prior to transfusion are desirable because of their speed and simplicity. This is especially true when combined with the Coca technic for direct matching. If these methods are to be used safely, unusually high titered test serums must be employed in order

TABLE 2.—Comparison of Agglutinin Titer of Processed and Unprocessed Serum

Serum	Amount, Cc.	Anti Cells Whole Blood, Cc.	Macroscopic Agglutination Time
Unprocessed.....	0.05	0.05	20 seconds
Processed.....	0.05	0.05	4 seconds
(One fourth of original volume)			
Processed.....	0.05	0.05	20 seconds
(Rediluted to original volume)			

to detect clearly weak A and B cell factors. Serums of inadequate titer may be artificially concentrated by the lyophile method. This provides a more unlimited source of supply than has been previously available for use in open macroscopic methods for grouping.

Hemoglobin and Hemocyanin.—Higher animals all have blood containing iron-bearing hemoglobin, to act as an oxygen carrier. Instead of hemoglobin some of the lower sea animals have hemocyanin, which is almost the same chemical composition except that copper has been substituted for the iron. The green chlorophyll of plants, which promotes the reactions of photosynthesis which make all life possible, has a chemical composition quite similar to our own hemoglobin, but magnesium has been substituted for iron in the molecule.—Furnas, C. C. and Furnas, S. M.: Man, Bread and Destiny, New York: Reynal & Hitchcock, 1937.

Special Article

VITAMIN C

PHARMACOLOGY AND THERAPEUTICS

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This article and others recently published or to be published comprise a new series on the present status of our knowledge of the vitamins. They have been prepared under the general auspices of the Council on Pharmacy and Chemistry and the Council on Foods. The opinions expressed are those of the authors and not necessarily the opinions of either council. Reprints are not available but the articles will be published later in book form.—Ed.

Vitamin C is specifically involved in the prevention or treatment of scurvy. Since this factor was isolated, its structure determined and the pure substance synthesized, considerable advances in our knowledge of the physiology of vitamin C have been made and some evidence of the value of this substance in conditions other than scurvy has been developed. Exact knowledge of the pharmacologic action of vitamin C is still rather limited, but it is growing rapidly because of the development of chemical methods for estimating vitamin C in foods and body tissues and fluids. The present review is an attempt to summarize this knowledge as well as the present status of our knowledge of the therapeutic usefulness of vitamin C.

AVAILABLE PREPARATIONS OF VITAMIN C

It must not be forgotten that vitamin C is an accessory food substance and that ordinarily foods are relied on for a supply of this essential factor. As described in the paper on sources of vitamin C,¹ there are some foods which are especially potent. Chief among these are the citrus fruit juices, which long have been used in the prevention and treatment of scurvy. Fresh orange juice contains on the average from about 40 to 60 mg. of vitamin C per hundred cubic centimeters. The daily requirements of an adult are considered to be about 25 mg. for the prevention of scurvy and more than that for normal requirements. The exact requirements for normal health are not known but nutritionists have estimated that a standard allowance for an adult would be from 600 to 1,200 international units, equivalent to from 30 to 60 mg. of vitamin C. Canned tomato juice is also a rich source of vitamin C, as are the canned citrus fruit juices.²

It is customary to give vitamin C to all babies early in life. This is usually administered in the form of fresh orange juice, beginning even as early as the third week of life with a teaspoonful and, if well tolerated, increasing gradually until the baby is taking about 2 ounces daily by the third month. On this basis the infant will be receiving up to about 25 mg. or more of vitamin C a day. Other sources of vitamin C may be substituted for the fresh orange juice and this substitution should be on the basis of the vitamin C content.

Synthetic preparations of crystalline vitamin C are now available. Ascorbic acid is freely soluble in water and may be administered orally in tablet form or dissolved in water. For parenteral use, either intramuscularly or intravenously, Fisher and Leake³ have recommended that ascorbic acid be dissolved in sterile water and neutralized with one-half its weight of sodium bicarbonate immediately before injection. If this procedure is followed, the vitamin will not lose in potency and local reaction will be avoided.

Before the isolation of the crystalline vitamin, doses larger than 500 mg. daily (approximate content of 1 quart of orange juice) were impracticable. We have noted in some of our experimental work that certain persons will not tolerate even 1 pint of orange juice daily. Since the crystalline vitamin has become available, it may be used to supplement the dietary intake or to be given in large doses.

The crystalline vitamin has an indicated therapeutic value in infant feeding under certain conditions. There are some infants who are allergic to or intolerant to fruit juices and other foods rich in vitamin C. This intolerance or sensitivity is presumably due to the proteins of the juices or foods containing the natural vitamin, and in such cases the crystalline vitamin may be advantageously substituted. The substitution of the crystalline vitamin for the natural food sources may also have a therapeutic indication in certain acute and chronic gastrointestinal diseases in which adequate absorption of vitamin C from natural food sources is altered or interfered with.

In certain of the conditions to be discussed, relatively large doses of crystalline vitamin C are required to obtain therapeutic effects. Although the normal daily human requirements have been estimated to be from 15 to 40 mg. or even up to 60 mg.,⁴ it is difficult to explain why certain therapeutic effects can be obtained only by administering doses of from ten to twenty-five times this amount. Our present state of knowledge is so limited that a precise statement of what constitutes proper dosage is not practicable. In New and Non-official Remedies it has been suggested that crystalline vitamin C be administered in quantities of 10 mg. for the prevention of infantile scurvy. "The therapeutic dose is about 30 mg. daily, although many physicians prefer to administer larger amounts to adults."⁵

One question raised with regard to the higher dosages that are possible with crystalline vitamin C is the possibility of toxicity. It is rather generally accepted that vitamin C is nontoxic when administered in moderate doses to the human being and excess amounts are excreted. Repeated doses of as much as from 1 to 6 Gm. have been administered orally and intravenously to adults, with no evidence of toxic action.⁶ Friedman, McGoe and Ralli⁷ in a study of vitamin C clearance have repeatedly obtained plasma concentrations ranging from 5 to 22 mg. per hundred cubic centimeters (normal values are from 0.7 to 1.5 mg.) with no evidence of toxicity. However, Schade⁸ observed vagotonic

3. Fisher, B. H., and Leake, C. D.: The Parenteral Administration of Cevitamic Acid (Ascorbic Acid) Solution, *J. A. M. A.* **103**:1556 (Nov. 17) 1934.

4. Smith, Sybil L.: Vitamin C Nutrition and Requirements, *J. A. M. A.*, to be published.

5. New and Nonofficial Remedies, Chicago, American Medical Association, 1938, p. 472.

6. Personal clinical experience.

7. Friedman, G. J.; McGoe, C., and Ralli, E. P.: Personal communication to the authors; abstract, *Proc. Am. Physiol. Soc. Bull.*, 1938.

8. Schade, H. A.: Beitrag zur Frage des Einflusses von Vitamin C (1-Ascorbinsäure) auf Pigmentierungsvorgänge, *Klin. Wchnschr.* **14**: 69 (Jan. 12) 1935.

From the Northwestern University Medical School.
1. Bessey, Otto A.: Vitamin C: Methods of Assay and Dietary Sources, *J. A. M. A.* **111**:1290 (Oct. 1) 1938.
2. The Vitamin C Content of Commercially Canned Tomato Juice and Other Fruit Juices as Determined by Chemical Titration: A Report of the Council on Foods, *J. A. M. A.* **110**:650 (Feb. 26) 1938.

symptoms in growing children at the height of the vitamin C action (fatigue, exhaustion, slow pulse, increased intestinal peristalsis). Widenbauer⁹ noted vagotonic symptoms such as dermatographia, hyperemia, erythema, increased peristalsis and bradycardia in infants on maximum doses of vitamin C. These symptoms were not attributed to a hypervitaminosis but to drug sensitivity or idiosyncrasy to ascorbic acid. In the guinea pig Randoin¹⁰ has noted that, if a scorbutic animal is given relatively large quantities of vitamin C, the animal may lose weight and the symptoms of scurvy reappear.

FUNCTIONS AND PHARMACOLOGIC ACTIONS

The chief function assigned to vitamin C in the body is concerned with the formation of colloidal intercellular substances.¹¹ The intercellular substances which appear to be regulated by vitamin C are of mesenchymal origin—the collagen of all fibrous tissue structures, all non-epithelial cement substances, including the intercellular

were used, no evidence of vitamin C formation could be found. These authors concluded that animals which do not require a dietary supply of vitamin C synthesize ascorbic acid from dextrose in the intestine.

Occurrence in Body Fluids.—Vitamin C has been found in the body fluids. It is excreted in the urine, the amounts varying with the dietary intake.¹⁴ The level of vitamin C in the blood plasma also varies directly with the dietary intake¹⁵ (chart 1). The methods for chemical assay of the blood plasma have been given in another article of the series.^{15a} In our opinion the recommendation that potassium cyanide be used as a stabilizer of ascorbic acid is unfortunate. We and others^{15b} have recently shown that potassium cyanide not only does not prevent the loss of ascorbic acid from the blood plasma, but its use may also give erroneous results of considerable magnitude. The use of potassium cyanide in carrying out the method for determining ascorbic acid in blood should be discontinued. Low blood plasma values found in man have been associated with active scurvy.¹⁶ In the scorbutic guinea pig the lowest plasma values have occurred just before death.¹⁷ According to Borsook,¹⁸ practically all the ascorbic acid in plasma and serum is in the reduced state.

Plaut and Bülow¹⁹ have observed a direct relationship between the vitamin C content of the cerebrospinal fluid and the dietary intake, which corresponds to the observations on blood plasma. Stuteville²⁰ noted the presence of vitamin C in saliva. Abt, Farmer and Epstein²¹ measured the ascorbic acid content of saliva obtained from students, before and after diets supplemented by vitamin C. No definite relationship could be established between the dietary intake and the salivary content. The salivary level was also found to be independent of the level in the blood. According to Zimmet and Dubois-Ferrière,²² the concentration of vitamin C in the saliva of children increased progressively from a level of 0.04 mg. per hundred cubic centimeters at 4 years of age to 0.11 mg. per hundred cubic centimeters at 16 years.

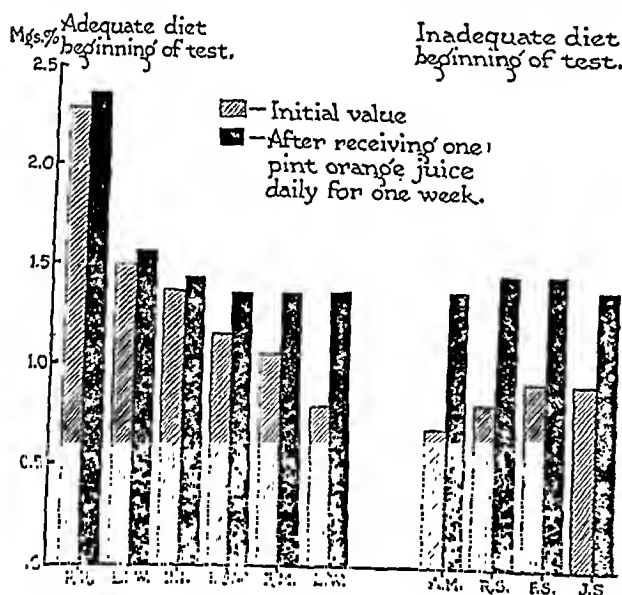


Chart 1.—Vitamin C content of the blood as influenced by diet: ascorbic acid values of young adults.

substance of the capillary wall, dentin, cartilage, and the matrices of bone. It has also been suggested that vitamin C may function as a respiratory catalyst, aiding cellular respiration by acting as a hydrogen transport. The theory suggesting this function has received support in relation to plant and vegetable life¹² but has not been proved for animal tissue.

It has been shown that man, the guinea pig and the primates are incapable of synthesizing vitamin C. In tissue slice experiments, Widenbauer and Korschoreck¹³ reported an increase in vitamin C, as measured by iodine titration, when slices of intestine from the mouse or rat, animals which are capable of synthesizing vitamin C, are incubated in a sterile dextrose-salt medium. When slices of liver, spleen, stomach or brain

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12. Szent-Györgyi, Albert: On the Function of Hexuronic Acid in the Respiration of the Cabbage Leaf, *J. Biol. Chem.* 90: 385 (Jan.) 1931.

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14. Harris, L. J.; Ray, S. N., and Ward, Alfred: The Excretion of Vitamin C in Human Urine and Its Dependence on the Dietary Intake, *Biochem. J.* 27: 2011 (Nov.) 1933. Harris, L. J., and Ray, S. N.: Diagnosis of Vitamin C Subnutrition by Urine Analysis, with Note on Antiscorbutic Value of Human Milk, *Lancet* 1: 71 (Jan. 12) 1933.

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16. Abt, A. F., and Epstein, I. M.: Cevitamic Acid in the Treatment of Infantile Scurvy, *J. A. M. A.* 104: 634 (Feb. 23) 1935.

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18. Borsook, Henry; Davenport, H. W.; Jeffreys, C. E. P., and Warner, R. C. P.: Oxidation of Ascorbic Acid, *J. Biol. Chem.* 117: 237 (Jan.) 1937.

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The vitamin C content of sweat,²³ aqueous humor²⁴ and gastric juice²⁵ has been determined. A study of the occurrence of vitamin C in the feces has been made in our laboratory.²⁶ In the normal individual not over 6 to 10 mg. daily are excreted, even with oral feeding of large amounts. Under abnormal conditions (diarrhea, colitis and the like) the amount depends largely on the number and type of stools. Ishibashi²⁷ has reported studies on the vitamin C content of the feces of infants. According to him, peroral administration of the vitamin produced no fecal rise.

Absorption and Excretion.—Vitamin C appears to be selectively absorbed by the tissues of the intestinal tract,²⁸ principally the small intestine. Klodt²⁹ believes that bile may aid absorption. In achlorhydria, blood plasma levels are usually lower than normal. This may be caused by decreased absorption of active vitamin C from the intestine, which in turn is caused by a lessened acidity of the intestinal contents or by a changed bacterial flora. In support of the latter view Kendall and Chinn³⁰ have shown that ascorbic acid is destroyed by certain bacteria isolated from stomach and intestinal contents of achlorhydric patients. Further evidence of the loss of vitamin C activity prior to absorption has been afforded by the observation of Wilder and Wilbur³¹ that variable amounts of vitamin C are lost in the stool or destroyed in the gastrointestinal tract even under normal conditions. Hou³² found that ascorbic acid administered by subcutaneous injection was twice as effective as that given by mouth in the protection of guinea pigs against scurvy. He has suggested as the probable explanation that part of the ascorbic acid administered orally is lost in the gastrointestinal tract. Until definite information is available to the contrary, it must be assumed that not only are there individual variations in absorption of vitamin C from the intestinal tract but also under certain conditions the absorption may be definitely abnormal.

After absorption vitamin C may be detected in increased quantities in the blood plasma, by which it is transported to the various tissues of the body. Whether a storage of vitamin C occurs in the animal body is still a debatable question.³³ This is indicated by the necessity for a continuous food supply in species incapable of synthesizing vitamin C. Because of the ease with which vitamin C can be determined chemically, many studies have been made concerning its metabolism. Large doses of the vitamin have been administered and measurements made of the amounts excreted in the urine. Johnson and Zilva³⁴ consider that "saturation" of the

tissues with vitamin C has been reached when the ingestion of a certain amount of vitamin C is roughly equaled by the daily excretion of the vitamin in the urine. Succeeding investigators have attempted to determine the saturation of the organism by oral or intravenous administration of test doses of ascorbic acid and subsequent measurement of its excretion in the urine. The majority of investigators employing urinary excretion tests have failed to recognize the possibility that absorption from the intestinal tract may not be complete.³⁵ Further, they have arbitrarily stated that various amounts ranging from 30 to 75 per cent of the test dose are excreted on reaching "a state of saturation." If subjects on a previous minimal vitamin C diet require a total of from 2,000 to 3,000 mg. of ascorbic acid before appreciable amounts are excreted in the urine, must it be assumed that the total amount of vitamin administered found its way to the tissues? It should be obvious that, before quantitative statements are derived, consideration must be given to questions of destruction in and absorption from the intestinal tract, and excretion by way of the feces.

We have repeatedly observed that, on the oral administration of large quantities of vitamin C, only small amounts are excreted in the urine, while a steady rise in plasma level occurs. If the oral ingestion is continued for a sufficient period, a point of plasma elevation will be attained, following which a rapid urinary excretion of a large part of the ingested ascorbic acid occurs. We believe that the plasma level at which this quantitative urinary excretion occurs shows considerable individual variation.

Everson and Daniels³⁶ state that ascorbic acid metabolism may be compared with nitrogen metabolism in that the urinary excretion of vitamin C is of both endogenous and exogenous origin. Hawley and others³⁷ report that the amount of vitamin C excreted in the urine may vary according to the acid-alkali content of the diet, a highly alkaline urine having lower amounts than a highly acid urine. Daniels³⁸ reports that therapeutic doses of acetylsalicylic acid increase the excretion of vitamin C in the urine of children, while Youmans³⁹ states that it does not increase or decrease excretion of vitamin C in the urine of adults. It has been reported by Ahmad⁴⁰ that diets high in protein and fat cause an increased urinary excretion of vitamin C. On the other hand, Heinemann⁴¹ noted that the total reducing power of the urine varies directly with the protein intake, while the vitamin C excretion remains uninfluenced.

Diuretic Effect.—Abbasy⁴² has noted that, following the administration of a test dose (700 mg. of ascorbic acid to 10 stone, 140 pounds, 63.5 Kg. of body weight), the volume of urine, as well as the excretion of vitamin

23. Cornbleet, Theodore; Klein, R. I., and Pace, E. R.: Vitamin C Content of Sweat, *Arch. Dermat. & Syph.* **34**: 253 (Aug.) 1936.

24. Rosner, Lawrence, and Bellows, John: Ascorbic Acid Oxidase in Determining Vitamin C in Lens and Aqueous Humor, *Proc. Soc. Exper. Biol. & Med.* **34**: 493 (May) 1936. Buschke, W.: Blutzirkulation im Auge und Vitamin C, *Arch. f. Augenh.* **109**: 691, 1936.

25. Peters, G. A., and Martin, H. E.: Ascorbic Acid in Gastric Juice, *Proc. Soc. Exper. Biol. & Med.* **36**: 76 (Feb.) 1937.

26. Farmer, C. J., and Chinn, Herman: Unpublished data.

27. Ishibashi, T.: Vitamin C of the Urine and Feces of Newly Born Infants, *Acta paediatr.*, Japan, **43**: 187 (Feb.) 1937.

28. Zilva, S. S.: Ascorbic Acid Content of Intestine of Guinea Pig, *Biochem. J.* **29**: 100 (Nov.) 1935.

29. Klodt, W.: Ueber den Einfluss der Galle auf die Vitamin C Resorption, *Med. Wch.* **10**: 477 (April) 1936.

30. Kendall, A. I., and Chinn, Herman: A Method for Isolation of Ascorbic Acid Fermenting Bacteria, *Proc. Soc. Exper. Biol. & Med.* **35**: 8 (Feb.) 1938; Decomposition of Ascorbic Acid by Certain Bacteria, *J. Infect. Dis.* **62**: 330 (May-June) 1938.

31. Wilder, R. M., and Wilbur, D. L.: Diseases of Metabolism and Nutrition, *Arch. Int. Med.* **59**: 512 (March) 1937.

32. Hou, H. C.: Comparison of Oral and Subcutaneous Administration of Protective Doses of Ascorbic Acid (Vitamin C), *Proc. Soc. Exper. Biol. & Med.* **33**: 1391 (June) 1935.

33. Zilva, S. S.: Vitamin C Requirements of the Guinea Pig, *Biochem. J.* **30**: 1419 (Aug.) 1936.

34. Johnson, S. W., and Zilva, S. S.: The Urinary Excretion of Ascorbic Acid and Dehydroascorbic Acids in Man, *Biochem. J.* **28**: 1393 (No. 4) 1934.

35. Storage of Vitamin C, editorial, *J. A. M. A.* **108**: 395 (Jan. 30) 1937.

36. Everson, G. J., and Daniels, A. L.: Vitamin C Studies with Children of Preschool Age, *Nutrition* **12**: 15 (July) 1936.

37. Hawley, E. E.; Frazer, J. P.; Button, L. L., and Stephens, D. J.: Effect of the Administration of Sodium Bicarbonate and of Ammonium Chloride on the Amount of Ascorbic Acid Found in the Urine, *Nutrition* **12**: 215 (Aug.) 1936.

38. Daniels, Amy L., and Everson, Gladys J.: Influence of Acetylsalicylic Acid (Aspirin) on Urinary Excretion of Ascorbic Acid, *Proc. Soc. Exper. Biol. & Med.* **35**: 20 (Oct.) 1936.

39. Youmans, J. B.; Corlette, M. B.; Frank, Helen, and Corlette, Mildred: Failure of Acetylsalicylic Acid to Affect Excretion of Ascorbic Acid (Vitamin C) in Urine, *Proc. Soc. Exper. Biol. & Med.* **36**: 73 (Feb.) 1937.

40. Ahmad, Bashir: Observations on Excretion of Vitamin C in Human Urine, *Biochem. J.* **30**: 11 (Jan.) 1936.

41. Heinemann, Martin: On Relation Between Diet and Urinary Output of Thiosulfate and Ascorbic Acid: Human Requirements for Vitamin C, *Biochem. J.* **30**: 2299 (Dec.) 1936.

42. Abbasy, M. A.: The Diuretic Action of Vitamin C, *Biochem. J.* **31**: 339 (Feb.) 1937.

C in the urine, showed a definite rise. He therefore attributed a diuretic action to the vitamin. As a result of an extended study of the urinary output of nine patients with cardiac disease, Evans⁴³ states that vitamin C was found to induce a greater diuresis than digitalis but less than theobromine, theobromine with sodium salicylate, and ammonium chloride.

Blood Pressure.—It was noted by Kasahara and Kawamura⁴⁴ that guinea pigs showed a rise in blood pressure when injected with 100 mg. per kilogram or greater doses of ascorbic acid and that monkeys showed a rise in blood pressure starting with injections of 40 mg. per kilogram and a greater rise with doses of from 100 to 200 mg. per kilogram. The authors conclude that the blood pressure rises in monkeys and guinea pigs following injections only of large amounts of ascorbic acid.

Capillary Action.—While it has been shown histologically that vitamin C regulates the intercellular substance of the capillary wall, a clear relationship between capillary resistance of the skin and dietary intake of vitamin C has not been definitely established.⁴⁵ Göthlin⁴⁶ has recently attempted to correlate capillary resistance measured by his positive pressure method with the ascorbic acid content of blood. He found increased capillary fragility in individuals with blood levels of 1 mg. per liter or less. In more than twenty cases of both infantile and adult scurvy observed by us, we have never obtained such low blood values.

Effect of Anesthesia.—According to Bowman and Muntwyler,⁴⁷ urinary excretion of vitamin C is increased following ether anesthesia in the dog, rat and guinea pig. The ascorbic acid content of the kidneys, liver, adrenals and spleen was found to be lessened after anesthesia. Bersin and his co-workers⁴⁸ found that excretion of ascorbic acid was diminished in the urine following ether and chloroform anesthesia in guinea pigs, on administration of a test dose of vitamin C intravenously.

RELATION OF VITAMIN C TO SCURVY

Scurvy is a disease for which vitamin C is the sole therapeutic agent. The specificity of vitamin C in scurvy was demonstrated long before the isolation of the vitamin and, as soon as the vitamin was available as a pure chemical substance, it was successfully used both clinically and experimentally in the treatment of scurvy. According to Finkle,⁴⁹ a low body level of vitamin C is etiologic for no other disease than scurvy, with the possible exception of lupus erythematosus. As has been previously stated, the blood plasma levels are extremely low in human scurvy. Abt,⁵⁰ in reporting his early studies on human scurvy, showed that the dietary history and clinical signs and symptoms parallel

the low blood plasma values and that the plasma content shows a rapid rise in a healing scurvy. With the aid of the micromethod described by us, tolerance tests were made on patients recovering from scurvy, the ascorbic acid content of the plasma being determined hourly and curves plotted. The initial level rises slightly but usually returns to a low level.⁵¹ As the patient continues on a high vitamin C intake, fasting blood levels on successive days attain higher values. Tolerance tests performed at these times by the oral administration of 10 mg. of ascorbic acid per kilogram of body weight show, with fair uniformity, a higher value at the peak of each succeeding curve. The peak is usually reached by the second hour, and the rise (difference between the initial fasting level and the value attained at the peak) increases until a state is attained in which the body promptly excretes the major part of the ingested ascorbic acid.

Ascorbic acid may be given intramuscularly or intravenously for the cure of scurvy when nausea, emesis or extreme prostration prevents its oral administration. It is interesting to note that Hess and Unger⁵² in 1918 administered neutralized orange juice intravenously to three patients for whom oral administration was impossible.

Jackson and Park⁵³ have reported a case of congenital scurvy. By determining the vitamin C content of the blood obtained simultaneously from the cord of the infant and the vein of the mother immediately after delivery, Abt, Farmer and Epstein²¹ found practically identical values from the two sources. From these observations it may be concluded that the fetus is dependent for its source of vitamin C on the maternal dietary. If the vitamin intake of the mother is extremely low during pregnancy, congenital scurvy may consequently result.

Goettsch⁵⁴ has noted in treating infantile scurvy that a single massive dose of vitamin C permits the healing of the scurvy as effectively as the same amount of vitamin in divided doses. Observing calcification of subperiosteal hematomas, she noted that healing commenced as early as the forty-eighth hour after the intravenous injection of the large doses of vitamin. Abt⁵⁵ reports that vitamin C is a factor in calcium deposition in the bones. Its addition to a scorbutic diet causes a rapid deposition of calcium at the epiphyseal ends of bones and in trabeculae. The effect is probably due to the necessity of adequate amounts of vitamin C for normal production of the organic matrix in which the lime salts are deposited.

Hess⁵⁵ has noted the development of scurvy in infants on a diet which contained sufficient vitamin to be ordinarily antiscorbutic. These infants recovered when given larger amounts of vitamin C orally. Hess felt that the development of scurvy in these cases was due to a failure of absorption of the ingested vitamin. Hagmann⁵⁶ reported that scurvy developed in a 2½ months old infant receiving 4 drachms (15 cc.) of orange juice daily. Large doses of vitamin C taken

43. Evans, William: Vitamin C in Heart Failure, *Lancet* 1:308 (Feb. 5) 1938.

44. Kasahara, M., and Kawamura, R.: Ueber den Einfluss der 1-Ascorbinsäure auf den Blutdruck, *Klin. Wchnschr.* 16:1543 (Oct.) 1937.

45. Abt, Farmer and Epstein.²¹ Wilder and Wilbur.³¹ Abbasy.⁴²

46. Göthlin, G. F.: When Is Capillary Fragility a Sign of Vitamin C Subnutrition in Man? *Lancet* 2:703 (Sept. 18) 1937; *Acta paediat.* 20:71, 1937.

47. Bowman, D. E., and Muntwyler, E.: Further Experiments upon the Excretion of Ascorbic Acid in the Urine Following Ether Anesthesia, *J. Biol. Chem.* 14:114, 1936; Ascorbic Acid Content of Tissue Following Ether Anesthesia, *Proc. Soc. Exper. Biol. & Med.* 35:587 (Jan.) 1937.

48. Bersin, T.; Lauber, H. J., and Nafziger, H.: Der Einfluss der Narkose und Operation auf den Vitamin C Haushalt, *Klin. Wchnschr.* 16:1272 (Sept. 11) 1937.

49. Finkle, Philip: Vitamin C Saturation Levels in Body in Normal Subjects and in Various Pathological Conditions, *J. Clin. Investigation* 16:587 (July) 1937.

50. Abt, A. F.: Newer Knowledge of Vitamin C, *Radiol. Rev. & Mississippi Valley M. J.* 59:106 (May) 1937.

51. Hess, A. F., and Unger, L. J.: Experiments on Antiscorbutic: Report of an Antiscorbutic for Intravenous Use, *Proc. Soc. Exper. Biol. & Med.* 15:141 (May) 1918.

52. Jackson, Deborah, and Park, E. A.: Congenital Scurvy: Case Report, *J. Pediat.* 7:741 (Dec.) 1935.

53. Goettsch, Elvira: Treatment of Infantile Scurvy with Cervantine Acid, *Am. J. Dis. Child.* 49:1441 (June) 1935.

54. Abt, J. C.: The Use of Calcium and the Choice of a Calcium Salt, *J. A. M. A.* 109:1276 (Oct. 16) 1937.

55. Hess, A. F.: Infantile Scurvy, in *System of Pediatrics* (I. A. Abt, Editor), Philadelphia, W. B. Saunders Company, 1923, vol. II, chapter 30, p. 842.

56. Hagmann, E. A.: Active Scurvy in an Infant Receiving Orange Juice, *J. Pediat.* 11:480 (Oct.) 1937.

orally failed to cure the scurvy, while vitamin C given intravenously caused an effective therapeutic response. Hagmann attributes the failure of the orally administered vitamin to effect a cure to a temporary faulty absorption from the gastrointestinal tract.

It has been noted that the urinary excretion of vitamin C in scurvy is low. Schultzer⁵⁷ has recently reported an average daily excretion of 11 mg. in the urine of a scorbutic patient before treatment. After daily intravenous injections of 40 mg. of the crystalline vitamin, the twenty-four hour urinary excretion rose to 16 mg. in the second week and to 26 mg. in the fourth week. Schultzer points out that on the basis of earlier experience the oral administration of 15 mg. of vitamin C daily was considered an adequate protective dose. Since a daily intravenous injection of 40 mg. of the vitamin was found to be an adequate curative

Zilva,³³ employing the urinary excretion tests in experimental animals, casts doubt on the nature of this latent condition.

In our work we have repeatedly pointed out that fasting blood plasma levels parallel the vitamin C intake. In healthy individuals on what is considered an adequate vitamin C intake the blood plasma value will be 0.7 mg. per hundred cubic centimeters or above. Blood plasma values below 0.7 mg. per hundred cubic centimeters are subnormal or at least suboptimal. Active scurvy may occur with values ranging up to 0.4 to 0.5 mg. per hundred cubic centimeters (chart 2). Most authors reporting on blood plasma determinations are in close agreement with these figures with the exception of Ingalls,⁶⁰ whose figures are very low: from 0.15 to 0.30 mg. per hundred cubic centimeters of blood plasma in asymptomatic scurvy and from 0 to 0.15 mg. in

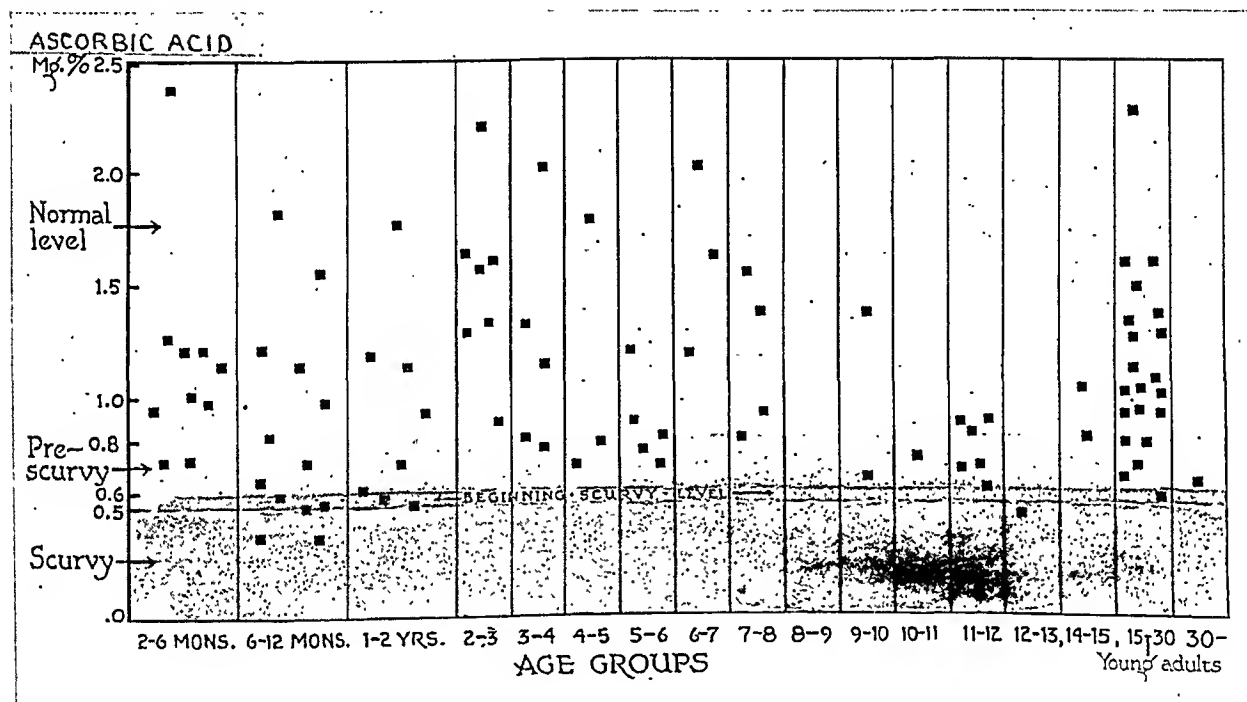


Chart 2.—Range of blood values for different age groups on adequate and subnormal diets, and in patients with scurvy.

dose, he suggests that the daily human requirement may be less than 40 mg. It has been⁵⁸ pointed out that, in the guinea pig, parenterally administered vitamin C is approximately twice as effective as a similar dose given orally.

LATENT SCURVY

The question of a prescorbutic state or latent scurvy was first emphasized by Hess⁵⁹ in 1917. It was his contention that this state might be analogous to latent tetany. Hess and succeeding observers attempted to demonstrate this condition by the use of various tests for capillary fragility in the skin. Since the chemical isolation of the vitamin, various observers have attempted, through urinary excretion tests, to demonstrate this condition. As we have previously stated,

active scurvy. The low values obtained by this author may be due to the fact that potassium cyanide^{15b} was added to the blood, which was in some cases permitted to stand instead of being immediately deproteinized with metaphosphoric acid and titrated with 2:6 dichlorophenolindophenol. It remains for future investigation to prove or disprove the existence of a latent or prescorbutic state. With respect to the development of human scurvy, it should be emphasized that scurvy may surreptitiously develop in patients under treatment for other conditions, if adequate protective vitamin C content of the diet has been overlooked.

ANEMIA AND VITAMIN C

Mettier, Minot and Townsend⁶¹ reported that anemia is commonly found in adults with a vitamin C deficiency. They believe that vitamin C can have a

57. Schultzer, P.: Saturation of a Scurvy Patient with Small Doses of Ascorbic Acid, *Biochem. J.* **31**:1934 (Nov.) 1937. Aht, A. F., and Farmer, C. J.: Exhibit on Vitamin C, Kansas City Session A. M. A., May 1936.

58. Hou, Z. Wright, I. S.; Lilienfeld, Alfred, and MacLenathen, Elizabeth: Determination of Vitamin C Saturation, *Arch. Int. Med.* **60**: 264 (Aug.) 1937.

59. Hess, A. F.: Subacute and Latent Infantile Scurvy: The Cardio-respiratory Syndrome (A New Sign), *J. A. M. A.* **68**:235 (Jan. 27) 1917.

60. Ingalls, T. H.: Studies on Urinary Excretion and Blood Concentration of Ascorbic Acid in Infantile Scurvy, *J. Pediat.* **10**:577 (May) 1937.

61. Mettier, S. R.; Minot, G. R., and Townsend, W. C.: Scurvy in Adults, Especially Effect of Food Rich in Vitamin C on Blood Formation, *J. A. M. A.* **95**:1089 (Oct. 11) 1930.

specific effect on erythropoiesis when there has been a chronic lack of this vitamin. Anemia is more frequently associated with scurvy in the adult than in the infant, judging from clinical reports. Alfred Hess⁶² noted that anemia was not constantly associated with infantile scurvy; in fact, in some of his scorbutic infants he reported a polycythemia. Rohmer and Bindschedler⁶³ reviewed the literature, noted the disagreement of the various authors on the association of anemia with infantile scurvy, and concluded that anemia is not an essential symptom of vitamin C deficiency. Hans Aron⁶⁴ also reported that anemia is not always associated with scurvy and that when it occurs it is not due to loss of blood, as was formerly believed. He stated also that in many instances it is difficult to determine whether one is dealing with a scurvy accompanied by anemia or an alimentary anemia complicated by scurvy. Parsons and Hawksley⁶⁵ suggested that hemopoiesis does not occur in the absence of vitamin C. They believed that in some cases of deficiency anemia more than one factor may be lacking and stated that "a child suffering from nutritional anemia may also develop scurvy, and the anemia of scurvy, in which case for its complete cure vitamin C as well as iron will be required." It is the opinion of Cooley⁶⁶ that there is no direct relationship between any of the avitaminoses and a definite type of anemia. Gingold⁶⁷ concluded that ascorbic acid has no effect on the normal or pathologic hemopoietic organs and is not, therefore, indicated in the treatment of pernicious anemia, secondary anemias or leukemias.

We have recently noted a 10 months old infant suffering with scurvy who was being fed on a diet containing a mixture of numerous proprietary products, so that the diet was high in calcium, iron and vitamins A, B₁ and D; the diet lacked only vitamin C. The infant was of a ruddy complexion, the red blood count was 4,800,000 and the hemoglobin 75 per cent (Sahli). The conditions in the case corresponded to our experimental experience with young guinea pigs, namely that anemia does not develop either clinically or experimentally when an adequate supply of iron is present in the scorbutic diet. When anemia accompanies lack of vitamin C it is probably due to a generally deficient diet in which substances other than vitamin C, especially iron, have been lacking. An accompanying infection may be a causative factor in the production of such anemia. While it is felt by some that the anemia of vitamin C deficiency may be one of commission, the result of a dysfunctioning of the red blood cell-forming elements, it is probably more often a condition produced by omission, namely of iron, in the generally deficient diet.

Heilmeyer⁶⁸ injected iron ascorbate intravenously in patients suffering from secondary anemia and noted

good results, especially in those patients in whom oral administration of iron was interfered with by metabolic disturbances. He further administered iron ascorbate orally and noted a better absorption with this preparation than with other iron products. He was able to obtain a full iron effect with doses of from 300 to 600 mg. daily. Glanzmann⁶⁹ has recommended iron ascorbate in the treatment of infantile anemia of the alimentary type. Pijoan⁷⁰ later made a similar report. It is evident that the need of a preparation such as iron ascorbate is limited.

LEUKEMIA AND VITAMIN C

Stephens and Hawley⁷¹ have noted that the vitamin C content of leukocytes is considerably greater than that of the plasma or erythrocytes. They noted an extremely high value for the ascorbic acid of the whole blood in leukemias. Eufinger and Gaehgans⁷² have reported the treatment of a case of myeloid leukemia in which the white count was brought back to normal by the injection of 2,000 mg. of ascorbic acid.

RELATION OF VITAMIN C TO HEMORRHAGIC DISEASES

Following the isolation of vitamin C in crystalline form there was a great impetus for investigations of its therapeutic value in hemorrhagic diseases and hemorrhage in other diseases. At first, numerous reports appeared claiming good results from the use of vitamin C in symptomatic purpura, thrombopenic purpura, Schönlein's and Henoch's purpuras, and hemophilia. Favorable claims also were made for such conditions as leukemia, acute hemorrhagic nephritis, metrorrhagia, pulmonary and gastric hemorrhages, and intestinal hemorrhage in ulcerative colitis and following perforations in typhoid. These were usually accounts of success in isolated cases.⁷³ It soon became evident that these early enthusiastic claims could not be substantiated.

In examining several patients with thrombopenic purpura whose blood components had been studied for a considerable time prior to the therapeutic attempts with vitamin C, we were able, with Dr. Mila Pierce,⁷⁴ to demonstrate no appreciable improvement in the thrombopenia. The capillary resistance of the skin remained abnormally low after the administration of large doses of vitamin C both orally and intravenously. Several investigators⁷⁵ in this country have similarly been unable to report beneficial effects after treatment with vitamin C in cases of true thrombopenic purpura and hemophilia.

69. Glanzmann, E.: Zur Behandlung der Kinderanämien mit ascorbisauren Eisen, Schweiz. Med. Wchnschr. 67: 436 (May 15) 1937.

70. Pijoan, M.: Antiscorbutic Properties of a Salt of Iron and Ascorbic Acid, Science 86: 80 (July 23) 1937.

71. Stephens, D. J., and Hawley, E. E.: Partition of Reduced Ascorbic Acid in Blood, J. Biol. Chem. 115: 653 (Oct.) 1936.

72. Eufinger, H., and Gaehgans, G.: Ueber die Einwirkung des Vitamins C auf das Pathologisch veränderte weisse Blutbild, Klin. Wchnschr. 15: 150 (Feb. 1) 1936.

73. Boger, A., and Schröder, H.: Ueber die Stillung schwerster Blutungen bei allen Formen der hämorrhagischen Diathese und der Hemophilie durch parenterale Zufuhr von C-Vitamin, München. med. Wchnschr. 81: 1335 (Aug. 24) 1934. Vogt, E.: Ueber die Behandlung gynäkologischer Blutungen mit Vitamin C, ibid. 82: 263 (Feb. 14) 1935. Engelkes, N.: Treatment of Hemorrhagic Disorders with Vitamin C, Lancet 2: 1295 (Dec. 7) 1935.

74. Abt, A. F.: Physiology of Ascorbic Acid in Normal and Abnormal States, J. Physiol. U. S. S. R. 22: 807 (July) 1937.

75. Wright, I. S., and Lilienfeld, Alfred: Pharmacologic and Therapeutic Properties of Crystalline Vitamin C (Cevitamic Acid) with Experimental Reference to Its Effects on Capillary Fragility, Arch. Int. Med. 57: 241 (Feb.) 1936. Stephens, D. J., and Hawley, E. E.: Relationship of Vitamin C to the Hemorrhagic Diatheses, J. Lab. & Clin. Med. 22: 173 (Nov.) 1936. Finkle, Philip: Vitamin C Saturation Levels in Body in Normal Subjects and in Various Pathological Conditions, J. Clin. Invest. 16: 587 (July) 1937.

62. Hess, A. F.: Scurvy, Past and Present, Philadelphia, J. B. Lippincott Company, 1920.

63. Rohmer, P., and Bindschedler, J. J.: L'anémie pré-scorbutique du nourrisson, Acta. pediat. 13: 399 (June) 1932.

64. Aron, Hans: Die Nahrungsschaden des Kindes, Berlin and Vienna, Urban und Schwarzenberg, 1928, p. 103.

65. Parsons, L. G., and Hawksley, J. C.: Studies in Anemias of Infancy and Early Childhood; Anhematopoietic Anemias (Deficiency Diseases of Erythron); Nutritional Anemia and Anemias of Prematurity, Scurvy and Celiac Disease, Arch. Dis. Childhood 8: 117 (April) 1933.

66. Cooley, Thomas B.: Practice of Pediatrics, Joseph Brennenmann, Editor, Hagerstown, Md., W. F. Prior Company, 1937, vol. III, chapter 16, p. 9.

67. Gingold, N.: The Action of Ascorbic Acid (Vitamin C) on the Hemopoietic Apparatus Under Normal and Pathologic Conditions (Exclusive of Hemorrhagic States), Sang 11: 392, 1937.

68. Heilmeyer, H.: Die Behandlung eisen empfindlicher Anämien mit Askorbinsauren Eisen, Deutsches Arch. f. klin. med. 179: 216 (Sept.) 1936.

In a recent review on the hemorrhagic states, Wits⁷⁶ corroborated the negative therapeutic effect of vitamin C in nonscorbutic hemorrhagic states. This author mentioned the possibility of scurvy being associated with a hemorrhagic disease, the disappearance of some of the symptoms following treatment with the vitamin being due to its effect on the associated scurvy. An interesting report by Neuweiler⁷⁷ concerns the vitamin C content of the blood serum of women during normal menstruation. In this study the author found that the vitamin C content of the blood serum did not vary during the menstrual periods of three normal women. Szent-Györgyi and others,⁷⁸ in their early work with impure preparations of vitamin C, believed that successful therapeutic effects were attained in some of the nonscorbutic hemorrhagic diseases. He and his co-workers subsequently isolated a flavin which they term "vitamin P" and which they believed was responsible for the effect. In a recent report they have stated that this substance requires for its activity the presence of traces of ascorbic acid and, in the entire absence of ascorbic acid, vitamin P is inactive. According to these results it may be concluded that pure vitamin C has a negative therapeutic action on hemorrhagic diseases of a nonscorbutic etiology. The evidence for the existence of vitamin P is doubtful, however, and it is clear that further work will have to be done in this field before conclusions can be reached.

RELATION OF VITAMIN C TO OTHER CONDITIONS

Teeth.—Because gingivitis and hemorrhage into the gums constitute such a striking symptom of scurvy, the claim that vitamin C has a direct relationship with the well-being of the teeth has been made for a long period. Hanke,⁷⁹ in a study on children, concluded that the addition of 1 pint of orange juice and the juice of one lemon to a diet lacking in vitamin C, but otherwise normal, led in many cases to disappearance of gingivitis and an arrest or a reduction of the intensity of dental caries. Keeton⁸⁰ has administered 400 mg. of vitamin C daily for four or five days prior to the extraction of a tooth and reported that the effect on healing is striking.

Most of the evidence that vitamin C is related to normal development of the teeth has been deduced largely from experimental work on the guinea pig. The incisor teeth of the guinea pig differ from those of man in that they are constantly growing. One is led to question, therefore, the permissibility of carrying over to man, without reservation, all experimental evidence on this point.

Fish and Harris⁸¹ in their recent work on guinea pigs hold untenable the view of the earlier writers, who noted the formation of "pulp bones" in partial vitamin C deficiency and regarded this occurrence as a type of neoplastic change. By use of a technic in which a series of deficient and normal diets were fed, they noted that vitamin C is necessary for promoting the

functional activity of formative cells such as the odontoblasts, ameloblasts and osteoblasts. They noted that in mild chronic vitamin C deficiency the "pulp bone" is the result of a partial degeneration of the odontoblasts, forming a sear tissue.

Wolbach⁸² has pointed out that in the growing teeth of guinea pigs a lack of vitamin C causes the formation of dentin to cease and the pulp to become separated from the dentin by a liquid presumably produced by the odontoblasts. In the healing process in guinea pigs the formation of dentin is resumed. Wolbach concluded that, in infants, teeth in the process of formation may possibly be affected by scurvy in a manner similar to that noted in the guinea pig, but that specific evidence of this in the human being is lacking. Hou⁸³ has reported similar observations in the scorbutic guinea pig. As evidence of a change in mineral content, Toverud⁸⁴ has shown that the incisor teeth of scorbutic guinea pigs contain less ash than those of normal animals. Furthermore, the ash is lower in calcium and higher in magnesium than that from teeth of normal controls. The older writers recognize the loosening of teeth in the scurvy of both man and animals, and Boyle, Bessey and Wolbach⁸⁵ more recently have pointed out that, besides striking alterations in tooth pulp and dentin, there may be changes in the periodontal soft and calcified tissues. They concluded that there may be two types of pyorrhea, a local inflammatory disease and a systemic process causing diffuse atrophy of the alveolar bone. This systemic type of pyorrhea, as it occurs in infantile scurvy, is similar to that found in guinea pigs on a vitamin C-deficient diet. In a limited number of patients with this type of pyorrhea, they have noted a correlation between low blood ascorbic acid values and rarefaction of the alveolar bone. They believe that a low vitamin C intake is an important factor in the production of this type of systemic pyorrhea. The authors made no statement as to the therapeutic effect which vitamin C might have on this type of pyorrhea. It is probable that the beneficial effects noted by Hanke after the addition of large amounts of orange juice were due to amelioration of this systemic type of pyorrhea known to be caused by deficiency of the vitamin. Although there is still a dearth of exact knowledge of vitamin C in its relation to dental and gingival disease in man, there is a general unanimity of opinion that an adequate intake of vitamin C is necessary for normal tooth growth and tooth structure, and the maintenance of healthy gums in man.

Eye.—Whether deficiency of vitamin C has any significance in the etiology of cataract has been a matter of dispute. Various workers have found that, as in other tissues of the body, the concentration of vitamin C in the crystalline lens of scorbutic guinea pigs is lower than normal.⁸⁶ Low values have been reported in the cataractous lens.⁸⁶ Some investigators have been able to produce cataract in some guinea pigs by feeding them

76. Wits, L. J.: The Hemorrhagic States, *Brit. M. J.* 2: 689 (Oct. 9) 1937.

77. Neuweiler, W.: Vitamin C-Spiegel in Blute und Menstruation, *Klin. Wchnschr.* 16: 926 (Sept. 4) 1937.

78. Szent-Györgyi, A.; Armento, S.; Bentsath, A.; Beres, T., and Rusznayk, S.: Ueber den Einfluss von Substanzen der Flavongruppe auf die Permeabilität der Kapillaren, *Vitamin P, Deutsche med. Wchnschr.* 62: 1325 (Aug. 14) 1936.

79. Hanke, Milton H.: Diet and Dental Health, University of Chicago Press, 1933, p. 143.

80. Keeton, R. W.: Relation of Metabolic Diseases to Dentistry, *J. Am. Dent. A.* 24: 1336 (Aug.) 1937.

81. Fish, E. W., and Harris, L. J.: The Effects of Vitamin C Deficiency on Tooth Structure in Guinea Pigs, *Phil. Tr. Roy. Soc. London*, 223B, 1933, p. 489.

82. Hou, H. C.: A Comparative Study of the Vitamin C Content of Several Varieties of Chinese Oranges, *Chinese J. Physiol.* 9: 223 (Aug. 15) 1935.

83. Toverud, G.: The Influence of Diet on Teeth and Bone, *J. Biol. Chem.* 58: 358 (Dec.) 1923.

84. Boyle, P. E.; Bessey, O. A., and Wolbach, S. B.: Experimental Alveolar Bone Atrophy Produced by Ascorbic Acid Deficiency and Its Relation to Pyorrhea Alveolaris, *Proc. Soc. Exper. Biol. & Med.* 30: 733 (June) 1937.

85. Von Euler, H., and Malmberg, M.: Ueber die Antiskorbutische Wirkung der Augenlinsen und über ihren Gehalt an Reduktoren und Sulfhydrylen, *Ztschr. f. physiol. Chem.* 230: 225 (Oct.) 1934. Johnson.

86. Von Euler, H., and Martius C.: Ueber den Gehalt der Augenlinsen und Sulfhydrylverbindungen und an Ascorbinsäure, *Ztschr. f. physiol. Chem.* 222: 65 (Oct.) 1933.

a scurvy-producing diet,⁸⁷ especially if the aqueous humor was drained by paracentesis, but others have not been able to repeat the experiment.⁸⁸ Vitamin C is present in the normal lens and vitamin C depletion might conceivably predispose the lens to a greater degree of susceptibility to agents causing cataract which ordinarily do not affect the normal eye. Bellows⁸⁹ has studied the level of vitamin C in the blood of cataractous patients and found it to be definitely lower on the average than that of noneataractous persons of similar social status and age group (from 60 to 80 years).

Skin.—Vitamin C apparently has a definite relation to pigmentation of the skin. A lessened pigmentation in patients suffering with Addison's disease has been observed⁹⁰ after vitamin C had been administered for some time. Schroeder and Einhauser⁹¹ administered 300 mg. of vitamin C intravenously for fourteen days and noticed a decreased pigmentation of the face in a case of pernicious anemia. Cornbleet⁹² noted that the excess pigment in the skin in Addison's disease and in scurvy is absorbed when vitamin C is administered. Volpe⁹³ treated several patients suffering with psoriasis with large doses of ascorbic acid and noted striking improvement. We ourselves have noted depigmentation of the skin following massive vitamin C therapy in Addison's disease. In the case of a Negro, a daily oral dose of 450 mg. over a period of several months produced a noticeable mottling depigmentation below the eyes. It should be noted that large doses, far beyond the normal requirement, have been used to produce these therapeutic results.

The suggestion has been made⁴⁰ that vitamin C may be specific in lupus erythematosus as well as in scurvy.

ENDOCRINE DISTURBANCES

Several observers have pointed out the possibility of a relationship between ascorbic acid and thyroid gland function. Demole and Ippen⁹⁴ have demonstrated that loss of weight in guinea pigs on a scorbutic diet could be checked by the administration of 0.5 mg. of ascorbic acid daily. If, however, the animals received 0.1 mg. of thyroxine subcutaneously, the weight loss continued until the amount of daily oral ascorbic acid administration had been raised to from 10 to 20 mg. Demole and Ippen interpreted this as evidence of the antithyrotropic action of ascorbic acid. Heyl⁹⁵ has reported a morphologic change in the thyroid gland induced by ascorbic acid similar in appearance to that obtained by the injection of the thyrotropic hormone of the anterior pituitary lobe. If the extract of the anterior pituitary is subjected to oxidative processes, shown by control experiment to be severe enough

to destroy ascorbic acid, the pituitary extract still remained active. The author concluded that, in the case of the thyrotropic action of the anterior pituitary, a substance other than vitamin C is concerned. Spence and Scowen⁹⁶ have shown that the daily administration of large doses of ascorbic acid does not prevent the occurrence of thyroid hyperplasia in guinea pigs receiving injections of extract of anterior pituitary containing thyrotropic hormone. Marine and his associates⁹⁷ have noted the protective action of ascorbic acid against hypertrophy of the thyroid gland in guinea pigs injected with the thyrotropic factor. Sure and Theis⁹⁸ indicate that in experimental hyperthyroidism produced in rats by feeding toxic doses of thyroxine a vitamin C disturbance occurred as evidenced by the reduction of the vitamin C content of the adrenal, the thymus and the kidney, similar to that encountered in scurvy in the guinea pig. According to Paal and Brecht,⁹⁹ the administration of thyroxine and thyrotropic hormone to guinea pigs and rats leads to a rise in the ascorbic acid content of the adrenal gland and liver. When cortical extract free from ascorbic acid was given together with these substances, no such rise occurred. These controversial reports indicate the need for further experimental work on the relationship between vitamin C and the thyroid gland.

The relationship of vitamin C to dextrose tolerance in the guinea pig was studied by Sigel and King;¹⁰⁰ successive stages of vitamin C depletion induced a corresponding rise in the fasting blood sugar level and a distinctly lowered dextrose tolerance. Pfleger and Scholl¹⁰¹ have noted that in diabetic patients saturation with vitamin C intensifies the action of insulin, so that the carbohydrate metabolism of the patient could be regulated with smaller doses of insulin. They also noted that increased vitamin C ingestion lessened fatigue in diabetic patients.

The relationship between vitamin C and Addison's disease has been studied. As shown by Harris and Ray,¹⁰² both the cortex and the medulla of the normal adrenal gland have a high ascorbic acid content. In three cases of Addison's disease studied by Wilkinson and Ashford,⁹⁰ using the urinary test of Harris and Ray, there appeared to be a vitamin C subnutrition. Wilkinson's patients were being simultaneously treated with small doses of adrenal cortex extract and vitamin C. On this combined therapy a decrease in pigmentation of the skin was noted in two cases three months after discharge. Hoff¹⁰³ has also noted a decrease in pathologic pigmentation in Addison's disease.

In two patients with Addison's disease brought to our laboratory by Dr. Carl Johnson, daily oral administration of 450 mg. of ascorbic acid alone caused considerable depigmentation after from six to ten weeks but failed to improve other Addisonian symptoms. This

87. Monjukowa, N. K., and Frandkin, M. J.: Neue experimentelle Befunde über die Pathogenese der Katarakt, Arch. f. Ophth. 133: 378, 1935.

88. Johnson, S. W.: Cataract and Ascorbic Acid in Guinea Pig Eye, Biochem. J. 30: 1430 (Aug.) 1936.

89. Bellows, J. G.: Biochemistry of Lens; Cevitamic Acid Content of Blood and Urine of Subjects with Senile Cataract, Arch. Ophth. 15: 78 (Jan.) 1936.

90. Wilkinson, J. F., and Ashford, C. A.: Vitamin C Deficiency in Addison's Disease, Lancet 2: 967 (Oct. 24) 1936. Hoff.¹⁰³

91. Schroeder, H., and Einhauser, M.: Ueber einen Zusammenhang zwischen gestörter Vitamin-C-Resorption und pathologischer Pigmentierung bei Gastroenteritis und Achylagastria, München. med. Wchnschr. 83: 923 (June 5) 1936.

92. Cornbleet, Theodore: Vitamin C and Pigment, Arch. Dermat. & Syph. 35: 471 (March) 1937.

93. Volpe, I.: Ueber mehrer Erfolge in der Psoriasis Behandlung mit Vitamin C, Schweiz. med. Wchnschr. 67: 498 (May 29) 1937.

94. Demole, V., and Ippen, F.: Die Antithyrotropische Wirkung von Ascorbinsäure, Ztschr. f. physiol. Chem. 235: 226, 1935.

95. Heyl, J. G.: Thyreotroper Effekt von Vitamin C (Ascorbinsäure) und Unabhängigkeit der thyreotropen Wirkung des Hypophysen vorderlappens hervor, Acta brev. Neerland. 4: 12, 1934.

96. Spence, A. W., and Scowen, E. F.: The Effect of Ascorbic Acid on Experimental Goiter, Biochem. J. 29: 562 (Jan. 15) 1935.

97. Marine, David; Baumann, E. J., and Rosen, S. H.: Effect of Ascorbic Acid on Thyroid and Suprarenals of Guinea Pigs, Proc. Soc. Exper. Biol. & Med. 31: 870 (April) 1934.

98. Sure, Barnett, and Theis, R. M.: Hyperthyroidism and Vitamin C, Proc. Soc. Exper. Biol. & Med. 37: 646 (Jan.) 1938.

99. Paal, H., and Brecht, K.: Ascorbinsäure und Schilddrüsenfunktion, Klin. Wchnschr. 16: 261 (Feb. 20) 1937.

100. Sigel, A., and King, C. G.: Relationship of Vitamin C to Glucose Tolerance in Guinea Pig, J. Biol. Chem. 116: 489 (Dec.) 1936.

101. Pfleger, R., and Scholl, F.: Diabetes and Vitamin C, Wchnschr. Arch. f. inn. Med. 31: 169 (Oct. 31) 1937.

102. Harris, L. J., and Ray, S. N.: Vitamin C in the Suprarenal Medulla, Biochem. J. 27: 2006 (No. 6) 1933.

103. Hoff, F.: Beiträge zum Problem der krankhaften Hautpigmentierungen, Deutsche med. Wchnschr. 62: 129 (Jan. 24) 1936.

is in agreement with the observation of Siwe,¹⁰⁴ who also noted a decreased pigmentation without relief from the characteristic symptoms of Addison's disease.

GASTROINTESTINAL DISEASES

We have already referred to the subject of absorption, destruction and elimination of vitamin C in the gastrointestinal tract. Alt, Chinn and Farmer¹⁰⁵ found low blood values for vitamin C in patients suffering with achlorhydria. Einhauser¹⁰⁶ has reported an altered absorption of vitamin C in patients suffering with catarrhal gastro-enteritis. Although Stepp¹⁰⁷ points out that gastrointestinal disturbances can be the cause as well as the result of lack of vitamins, it is debatable whether a lack of vitamin C can be looked on as a direct contributing factor to gastric ulcer. In Schultzer's¹⁰⁸ studies the improbability of C-avitaminosis as an etiologic factor in peptic ulcer is pointed out. Harris, Abbasy, Yudkin and Kelly¹⁰⁹ and Archer and Graham¹¹⁰ reported low urinary excretion values for patients suffering with gastric ulcer. However, these low excretion values may have been related to the low dietary content of the diets prescribed for ulcer. Several investigators¹¹¹ have recently pointed out that the usual diets given patients suffering with peptic ulcer are likely to be deficient in vitamin C. The exact relationship of this dietary deficiency to hemorrhage from the ulcers is as yet unproved, although it would certainly seem advisable to supplement peptic ulcer diets with vitamin C. Portnoy and Wilkinson,¹¹² using urinary excretion, blood plasma level and intradermal tests, have shown a marked vitamin C deficiency in patients suffering from peptic ulcer. The severest degree of deficiency was found in patients with hematemesis. We ourselves have noted a mild scurvy develop in several patients on strict ulcer diets, because of a lack of vitamin C in the dietary.

Gaetgens¹¹³ has reported on hypovitaminoses of intestinal origin in pregnancy. He points out that there is an increased vitamin C requirement in pregnancy as the fetus gains its supply of ascorbic acid directly from the food intake of the mother. Gaetgens reports the case of a pregnant woman who, because of a severe ulcerative colitis and a restricted diet, acquired a severe deficiency of vitamin C, and he points out that, whenever gastrointestinal disturbances develop during pregnancy, it may be necessary to supply the maternal organisms with adequate amounts of vitamin C administered parenterally.

RELATION OF VITAMIN C TO IMMUNITY

A considerable amount of experimental work has been published with regard to the relationship of vitamin C to immunity, and this material has recently been comprehensively reviewed.¹¹⁴ It is not within the scope of this article to take up in detail all the reports covering this subject. Among the first observers to note an altered immunologic response when ascorbic acid was administered in sufficient doses were Sulzberger and Oser.¹¹⁵ These authors in a controlled experiment noted that large doses of ascorbic acid reduced and inhibited the susceptibility of the skin of the guinea pig to experimental sensitization with neoarsphenamine. Cornia¹¹⁶ noted that a high vitamin C diet should be of value to all patients receiving arsphenamine and that intensive therapy with vitamin C may be helpful in treating patients with post-arsphenamine dermatitis. Landfisch¹¹⁷ similarly reported that he was able to treat twenty-five patients who had previously shown definite sensitization to neoarsphenamine and marked symptoms of intolerance when the arsenical was administered alone by combining ascorbic acid injections with neoarsphenamine or by administering the ascorbic acid one-half hour before the neoarsphenamine. Further evidence of the increased tolerance of the organism for arsphenamine after ascorbic acid therapy has been reported recently by Dainow.¹¹⁸ Vitamin C is apparently of value in controlling the intolerance to arsenicals which must be intravenously administered.

Meyer¹¹⁹ believes that the toxic symptoms produced by chronic benzene poisoning may be due to an avitaminosis C. Experiments with guinea pigs showed that the toxic effect of an injection of 0.25 cc. of benzene four times a week was counteracted when a daily dose of 20 mg. of ascorbic acid was added to a scorbutic basal diet. As a possible mechanism for this effect, Vauthey¹²⁰ has recently suggested that ascorbic acid exerts a stimulatory effect on the liver, resulting in reduced toxicity of the chemical medicament.

Epstein¹²¹ noted that large doses of vitamin C aided in the desensitization of patients suffering with bronchial asthma. Jusatz,¹²² using rabbits on a deficiency diet, was able to augment the specific precipitant titer from ten to a hundred fold by adding ascorbic acid to each dose of horse protein intravenously injected. The oral administration of vitamin C failed to increase the specific precipitant titer. Madison and Manwaring¹²³ have confirmed Jusatz's experiments in rabbits using horse serum plus 100 mg. of crystalline vitamin C. These authors also noted

104. Siwe, S.: Das Verhalten der C-Vitamin bei Morbus Addisoni, *Klin. Wchnschr.* **14**: 1311 (Sept. 14) 1935.

105. Alt, H. L.; Chinn, Herman, and Farmer, C. J.: The Blood Cevitamic Acid in Patients with Achlorhydria, read before the Central Society for Clinical Research, Chicago, Nov. 5, 1937.

106. Einhauser, M.: C-Vitamin und Gastroenteritis, *Ztschr. f. d. ges. exper. Med.* **98**: 461, 1936.

107. Stepp, W.: Neue Gesichtspunkte in der klinischen Anwendung der rein dargestellten Vitamine, *Angewandte Chemie* **50**: 30 (Jan. 2) 1937.

108. Schultzer, P.: Studies on Capillary Resistance: Improbability of C-Vitaminosis as Etiologic Factor in Peptic Ulcer, *Acta med. Scandinav.* **83**: 555, 1934.

109. Harris, L. J.; Abbasy, M. A.; Yudkin, John, and Kelly, Simon: Vitamins in Human Nutrition: Vitamin C Reserves of Subjects of Voluntary Hospital Class, *Lancet* **1**: 1488 (June 27) 1936.

110. Archer, H. E., and Graham, George: The Scurvy State in Relation to Gastric and Duodenal Ulcer, *Lancet* **2**: 364 (Aug. 15) 1936.

111. Rivers, A. B., and Carlson, L. A.: Vitamin C as Supplement in Therapy of Peptic Ulcer: Preliminary Report, *Proc. Staff Meet., Mayo Clin.* **12**: 383 (June 16) 1937. Eusterman, G. B.: Peptic Ulcer; Medical Management, *Minnesota Med.* **20**: 766 (Dec.) 1937. Ingalls, T. H., and Warren, H. A.: A Symptomatic Scurvy, *New England J. Med.* **217**: 443 (Sept. 9) 1937.

112. Portnoy, Benjamin, and Wilkinson, J. E.: Intradermal Test for Vitamin C Deficiency, *Brit. M. J.* **1**: 328 (Feb. 12) 1938.

113. Gaetgens, G.: Die Beziehungen intestinal bedingter Hypovitaminosen zur Schwangerschaft, *Klin. Wchnschr.* **16**: 444 (March 27) 1937.

114. Robinson, E. C.: The Vitamins and Resistance to Infection, *Medicine* **13**: 123 (May) 1934. Perla, David, and Marmorston, Jessie: Role of Vitamin C in Resistance, *Arch. Path.* **23**: 543 (April) 1937; Role of Vitamin C in Resistance, *ibid.* **23**: 683 (May) 1937.

115. Sulzberger, M. B., and Oser, B. L.: Influence of Ascorbic Acid of Diet on Sensitization of Guinea Pigs to Arsphenamine, *Proc. Soc. Exper. Biol. & Med.* **32**: 716 (Feb.) 1935.

116. Cornia, F. E.: Experimental Arsphenamine Dermatitis; Influence of Vitamin C in Production of Arsphenamine Sensitiveness, *Canad. M. A. J.* **36**: 392 (April) 1937.

117. Landfisch, S.: Synthetische Ascorbic Acid New Auxiliary Remedy in Arsphenamine Therapy, *Polska gaz. lek.* **16**: 575 (July 18) 1937.

118. Dainow, I.: Intolerance aux arsenicénes et vitamin C, *Presse méd.* **45**: 1670 (Nov. 24) 1937.

119. Meyer, A.: Chronische Benzolvergiftung und Vitamin C, *Ztschr. f. Vitaminforsch.* **6**: 83 (Jan.) 1937.

120. Vauthey, M.: Vitamin C (1-Ascorbic Acid) and Tolerance for Chemical Medicaments, *Chem. Abstr.* **32**: 995 (Feb. 10) 1938.

121. Epstein, Alexander: Vitamin C in Desensitization; Advances in Vitamin Treatment, *Schweiz. med. Wchnschr.* **66**: 1087 (Nov. 7) 1936.

122. Jusatz, H. J.: Der Einfluss der Vitamine auf den Immunitätszustand des tierischen Organismus; wasserlösliche Vitamine, *Ztschr. f. Immunitätsforsch. u. exper. Therap.* **88**: 483 (Aug. 4) 1936.

123. Madison, R. R., and Manwaring, M. H.: Ascorbic Acid Stimulation of Specific Antibody Production, *Proc. Soc. Exper. Biol. & Med.* **37**: 402 (Nov.) 1937.

that, when the horse serum and ascorbic acid were injected separately, either at different times into the same vein or into different veins, the antibody stimulation was less pronounced than the effect obtained by mixing the horse serum and vitamin C before injection. Lemke¹²⁴ has reported that vitamin C, when injected intravenously into hypersensitive guinea pigs, desensitizes them. However, van Niekerk¹²⁵ states that vitamin C has no protective action for guinea pigs against anaphylactic shock to horse serum. He noted that no protective action resulted when the second dose of horse serum was combined with from 25 to 100 mg. of ascorbic acid. Hochwald¹²⁶ states that, if 100 mg. of vitamin C is injected into sensitized guinea pigs a few minutes before the shocking dose, no anaphylaxis develops. Solomonica¹²⁷ observed that, if his guinea pigs were injected with vitamin C prior to or during the sensitizing period, many of them survived. The protective effects of ascorbic acid were much lessened if the vitamin was given later, e.g. shortly before the shocking dose.

Vitamin C has recently been related to the complement content of the blood.¹²⁸ Ecker¹²⁹ and his co-workers have shown a definite correlation between the complement titer of guinea pig serum and the vitamin C content of the blood serum. When the animals were placed on a scorbutic diet the complement titer dropped, paralleling the decrease in ascorbic acid blood values. The values rose when vitamin C was fed to the scorbutic animals.

Jungeblut¹³⁰ noted that vitamin C, when added to tetanus toxin in vitro, inactivates the toxin though it fails to confer complete protection against tetanus intoxication in vivo. This author furthermore states that, as far as its in vitro action is concerned, vitamin C cannot be regarded as a specific detoxicant for any given virus or toxin.

It therefore seems probable that vitamin C, particularly when administered intravenously, is capable of protecting the body against certain drug intolerances, as noted for the arsenicals, of stimulating experimental antibody production, and perhaps of protecting against experimental anaphylaxis. The failure of oral administration is interesting and requires further experimental work for its explanation. The whole field of the relationship of vitamin C to natural resistance and immunity is but in its infancy, and much more experimental and clinical evidence must be accumulated before any definite therapeutic claims seem justifiable.

INFECTIONS AND INFECTIOUS DISEASES

Recent reviews suggest that a low vitamin C intake may be one of the causes of lowering natural resistance. There is evidence also that in the course of certain infections there is a greater demand for vitamin C.¹³¹

124. Lemke, H.: Beeinflussung des anaphylaktischen Shocks der Meer-schweinchen durch C-Vitamin, *Monatschr. f. Kinderh.* 67: 244 (Nov.) 1936.

125. van Niekerk, J.: Anaphylaxis and Vitamin C, *J. Allergy* 5: 446 (July) 1937.

126. Hochwald, A.: Allergiefragen und vitamin C, *Zentralbl. f. inn. Med.* 56: 769 (Sept. 21) 1935.

127. Solomonica, Bruno: Vitamin C and Anaphylactic Shock in Guinea Pigs, *J. Immunol.* 31: 209 (Sept.) 1936.

128. Vitamin C and Complement, editorial, *J. A. M. A.* 110: 2157 (June 25) 1938.

129. Ecker, E. E.; Pillemer, L.; Wertheimer, D., and Gradis, H.: Ascorbic Acid and Complement Function, *J. Immunol.* 34: 19 (Jan.) 1938.

130. Jungeblut, C. W.: Inactivation of Tetanus Toxin by Crystalline Vitamin C (1-Ascorbic Acid), *J. Immunol.* 33: 203 (Sept.) 1937.

131. The clinical reports have been most numerous. The reader is referred to the extensive bibliographies to be found in the review by Robinson¹³² and the reviews by Perla and Marmorston.¹³³

There have been numerous suggestive reports of the possible role of vitamin C in infectious diseases but the evidence is not yet clearcut. The effect of vitamin C on the integrity of the tissues is probably concerned with its role in the production of normal intercellular cement substances. This in turn may be prerequisite to the maintenance of natural resistance of the organism to infection.

Evidence showing the desirability of trying the effect of administering vitamin C, along with other treatment of infections, has been obtained chiefly by studying the vitamin C content of the blood plasma and the amount of vitamin C excreted in the urine. Low values for either or both have been observed in mild coryzal fever, acute pharyngitis, persistent chronic nasal sinusitis, chronic otitis media, acute respiratory infection, active osteomyelitis, rheumatoid arthritis, and rheumatic fever in children.

The administration of vitamin C has been tested in a number of disease conditions, and favorable reports have appeared in pneumonia, pertussis and rheumatic fever. Negative results have been reported in poliomyelitis, and the results are inconclusive in diphtheria.

It is evident that vitamin C is not a specific therapeutic agent in the treatment of any of these diseases. It should not be forgotten, however, that the importance of an ample diet has long been recommended in the treatment of febrile conditions, and such patients have perhaps an increased requirement for all of the vitamins.

WOUND HEALING AND SURGICAL CONDITIONS

Hans Aron⁶⁴ noted that in scorbutic children wounds of the skin often remained open without a tendency to heal. Following therapy with vitamin C, he observed that these wounds healed quickly. In a 6 weeks old infant whose laparotomy wound opened postoperatively, Lanman and Ingalls¹³² noted a definite early scurvy at autopsy. The authors then performed laparotomy on guinea pigs which had been on previous scorbutic diets. At intervals after operation the animals were killed and the authors report that the wounds broke down more easily in the scorbutic pigs than in the non-scorbutic controls. On histologic examination they noted defective repair of the corium and a poor production of collagen in the scars of the scorbutic animals. This is in agreement with the role which vitamin C plays in the formation of collagen. Taffel and Harvey¹³³ have recently confirmed the work of Lanman and Ingalls and expressed the opinion that vitamin C deficiency in man may indeed be one of the major causative factors in these cases of wound disruption where there is no evidence of infection of the wound. From the evidence presented one may conclude that vitamin C has an important role in the healing of surgical wounds. When a history of low vitamin C intake or a low plasma value is obtained preoperatively, it would seem logical to administer vitamin C preoperatively and postoperatively. Hanke¹³⁴ noted apparent acceleration of bone healing in fractures, following administration of vitamin C. Lauber, Bersin

132. Lanman, T. H., and Ingalls, T. H.: Vitamin C Deficiency and Wound Healing: Experimental and Clinical Study, *Ann. Surg.* 105: 616 (April) 1937.

133. Taffel, M., and Harvey, S. C.: Effect of Absolute and Partial Vitamin C Deficiency on Healing of Wounds, *Proc. Soc. Exper. Biol. & Med.* 38: 418 (May) 1938.

134. Hanke, H.: Experimentelle Untersuchungen über Beeinflussung der Knochenregeneration durch Vitamin C, *Deutsche Ztschr. f. Chir.* 245: 530, 1935.

and Nafziger¹³⁵ report an increased demand for vitamin C in infection of a surgical nature. Myerson¹³⁶ suggests that vitamin C deficiency is one of the possible factors in hemorrhage following tonsillectomy.

CONCLUSIONS

Vitamin C is definitely indicated as a therapeutic agent in the prevention and cure of scurvy. Whether vitamin C has a definite causal relationship to any other pathologic process is as yet uncertain. The vast amount of investigative and clinical research reported to date seems to be indicative of a further therapeutic role for vitamin C, though not enough progress has been attained to allow definite therapeutic conclusions to be formulated. Certain suggestive conditions may be briefly outlined when, aside from the prevention and cure of scurvy, vitamin C may be therapeutically indicated.

An ample supply is indicated in the diet of the pregnant woman and nursing mother. If the possibility of a prescurbutic state is accepted or if the existence of latent scurvy is recognized, it is imperative that adequate diagnostic methods and criteria be formulated in order to prevent the development of such states, which would be conditions of suboptimal nutrition and possibly deleterious to general health. We believe that fasting blood plasma values are to date the best method for determining the possibility of such a state. In order to prevent the occurrence of such a possibility, the minimal human requirement for vitamin C must be definitely known. Whether this requirement varies for different ages and different individuals is unknown.

The question of absorption following oral ingestion is of the utmost importance. Absorption has been entirely overlooked by most investigators and, when mentioned in the literature, has been discussed chiefly as a theoretical possibility. Little or nothing is known concerning the assimilation of vitamin C and its metabolism in abnormal and normal states. The implication that there is an increased need and an augmented metabolism for vitamin C in many infections is generally noted in all the numerous reports available. The exact proof for this important fact is lacking. How fever, toxemia and specific bacteria act on vitamin C in individual infections is still unknown. How vitamin C is absorbed, assimilated and utilized in specific infections is still unknown. The relation of vitamin C to the endocrines has been noted, and there are implications that it may be specifically related to hyperthyroidism, diabetes and Addison's disease. The exact facts are still lacking; this is more or less true of the other specific conditions here reviewed.

The failure of the oral administration of vitamin C in certain conditions in which its parenteral administration gives positive experimental or clinical results, and the positive results following its use in extremely large doses when its use in small doses was unavailing, are paradoxical questions which need elucidation.

Perhaps the value of a view on the therapeutic indications and implications for vitamin C at this time lies in its urge to spur us on to fill the gaps in our present knowledge which, it will be hoped, are as evident to the reader as they have been to the reviewers.

135. Lauber, H. J.; Bersin, T., and Nafziger, H.: *Der Ascorbinsäurebedarf bei chirurgischen Infektionen*, Klin. Wchnschr. 16:1274 (Sept.) 1937.

136. Myerson, M. C.: *Hemorrhage Following Tonsillectomy*, Am. J. Surg. 36:151 (April) 1937.

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Manufacturer.—Paley-Sachs Food Company, Houston, Texas.

Description.—Strained liver soup containing calf liver, carrots, potatoes, green peas, tomato purée, cabbage, celery, okra, onions, barley, brown rice and spinach, slightly seasoned with salt.

Manufacture.—The vegetables and cereal are prepared as described for Mrs. Paley's Baby Food—Strained Vegetable Soup with Beef Broth and Cereal (THE JOURNAL, Sept. 17, 1938, p. 1101). The liver is washed, skinned, and sieved raw. The strained liver, vegetables and cereals are thoroughly mixed, filled into jars, vacuum sealed and heat processed.

Analysis (submitted by manufacturer).—Moisture 83.1%, total solids 16.9%, ash 0.9%, fat (ether extract) 0.6%, protein (N \times 6.25) 4.6%, reducing sugars as dextrose 1.8%, sucrose (not determined), crude fiber 0.6%, total carbohydrates other than crude fiber (by difference) 10.2%, calcium (Ca) 0.004%, phosphorus (P) 0.021%, iron (Fe) 0.0009%.

Calories.—0.6 per gram; 17 per ounce.

NUTRADIET UNDILUTED TOMATO JUICE

Distributor.—The Nutradiet Company, a subsidiary of S & W Fine Foods, Inc., San Francisco.

Description.—Canned tomato juice without added salt retaining in high degree the original vitamin content.

Manufacture.—Vine-ripened, selected tomatoes on which no toxic spray has been used are washed, lightly scalded and pressed against a mesh screen to extract the juice, which is heated to 82 C. The cans are filled, sealed and processed at 85 C. for three minutes. All the equipment that comes in contact with the juice is made of stainless steel.

Analysis (submitted by manufacturer).—Moisture 93.3%, total solids 6.7%, ash 0.5%, fat (ether extract) 0.07%, protein (N \times 6.25) 1.1%, crude fiber 0.2%, carbohydrates other than crude fiber (by difference) 4.3%, titratable acidity (as malic and citric acids) 0.57%, vitamin C (titration) 12.8 mg. per 100 cc.

Calories.—0.22 per gram; 6 per ounce.

Vitamins.—76 international units per fluid ounce.

Claims of Manufacturer.—For use in special diets in which sugar or salt is proscribed or in quantitative diets of calculated composition.

SUNFILLED BRAND CONCENTRATED GRAPEFRUIT JUICE

Manufacturer.—Citrus Concentrates, Inc., Dunedin, Fla.

Description.—Canned concentrated grapefruit juice prepared from Florida grapefruit.

Manufacture.—The method is the same as that described for Sunfilled Brand Concentrated Orange Juice (THE JOURNAL, Aug. 20, 1938, p. 713).

Analysis (submitted by manufacturer).—Moisture 18.0%, total solids 82.0%, ash 2.8%, protein (N \times 6.25) 4.5%, reducing sugar as invert 41.7%, sucrose 18.3%, carbohydrates (by difference) 65.5%, citric acid 9.2%, vitamin C (iodine titration) 3.7 mg. per gram, specific gravity 1.40.

Calories.—2.80 per gram; 80 per ounce.

Vitamins.—The concentrate, when diluted with 9 parts of water by volume, furnishes approximately 996 international units of vitamin C per hundred grams of solution; when diluted with 11 parts of water by volume, the solution contains 830 units per hundred grams.

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

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SATURDAY, OCTOBER 22, 1938

THE AMERICAN PHARMACEUTIC INDUSTRY PROMOTES INTENSIVE RESEARCH

Within the past few years, leading corporations in the pharmaceutical industry have developed great laboratories to be devoted mainly to research. Several years ago Eli Lilly & Co. and Merck & Co. dedicated, with impressive ceremonies, well equipped laboratories for promotion of original investigations. Early in October the Abbott Laboratories and E. R. Squibb & Sons dedicated two large buildings. In the dedication of these laboratories many leaders in the field of scientific research, in medical education and in medical organization in the United States cooperated. Thus the speakers at the dedication of the Abbott Laboratories included the president of the Massachusetts Institute of Technology, the Surgeon General of the United States Public Health Service, leading investigators in research concerning the glands and the vitamins, and many others of note. In the dedication of the new Squibb laboratories, Nobel prize winners participated, as well as other distinguished educators and investigators. Apparently the American pharmaceutical industry is no longer the degenerate and spoiled child of medicine but has now become a real contributor to medical advancement. Certainly the contrast with the medicine of an earlier day is striking.

But a few decades ago the suggestion that a pharmaceutical house might spend vast sums of money on medical research, some of it of the type called "pure" research, would have been laughed to scorn. The pharmaceutical industry at the turn of the century was devoted largely to the manufacture of products included in the United States Pharmacopeia and to the promotion of "shot-gun" concoctions of chemicals and herbs sold with weird and extraordinary claims. The Food and Drugs Act of 1906, the establishment of the Council on Pharmacy and Chemistry of the American Medical Association and the regular reports of the Association's Bureau of Investigation had a significant effect in the

purification of this industry. Yet at the same time the advance on the part of progressive houses may well be credited not so much to these purifying factors as to scientific advancement in the field of therapeutics. Perhaps the most epoch making of all the discoveries that have been made were arsphenamine and insulin. Certainly Ehrlich's contribution was a stimulus to chemotherapy beyond any other of which we have knowledge, unless we include the new impetus given to this field by the development of sulfanilamide. Again the contribution of Banting and his co-workers of insulin stimulated research related to the active principles of the endocrine system. No doubt the possibilities associated with barbituric acid derivatives and the isolation of vitamins in pure form served also to a considerable extent to indicate to this great industry the possibilities for those who had something new to contribute.

Perhaps it would be folly to suggest that the great laboratories of research now associated with practically all the great pharmaceutical houses of this country have been built wholly out of philanthropic motives or out of that innate curiosity which animates the medical investigator. In these times competition is keen. Whenever a new product is discovered in any field, every pharmaceutical corporation endeavors to develop a product exclusively its own and preferably one for which claims may be made beyond those acceptable for the products manufactured by others. Thus the research laboratory may be expected from time to time to announce notable improvements over new products as rapidly as they come into use. Certainly everywhere at this time investigators are experimenting with sulfanilamide with the hope of developing new products of similar character with perhaps better action against certain bacterial organisms, perhaps lessened toxicity, perhaps greater efficiency. Out of such research may come some product of the utmost benefit to the medical profession and to the public.

The building of these great laboratories by the pharmaceutical industry indicates furthermore a confidence in the permanence of a free and independent medical profession. Certainly a medical profession subject to governmental interference or state control would result for pharmacy, as well as for medicine, in the hamstringing of progress. No doubt these great industries have tested the public pulse and have embarked on these new ventures with the feeling that the fundamental principles necessary to sound medical practice are vital to the life of man and that, even though they may be temporarily set aside, their truth will give them permanence. On a firm foundation like the scientific medicine of today, industry may well build to higher and higher things.

Since the fountain head of pure research has been in the universities, it is no more than right that the great commercial concerns should repay their debt by assuming their share of the burden.

DEATHS FOLLOWING ELIXIR OF SULF-
ANILAMIDE-MASSENGILL: VIII

About a year has passed since *THE JOURNAL* first announced the deaths which followed the administration of Elixir of Sulfanilamide prepared and sold by the S. E. Massengill Company of Bristol, Tenn. Preliminary tests at that time showed the poisonous fluid to consist essentially of 40 grains of sulfanilamide to the fluidounce of a menstruum containing approximately 72 per cent of diethylene glycol by volume, with flavoring. Week by week the number of deaths increased eventually to more than seventy-five. Within two weeks after the first editorial was published, the A. M. A. Chemical Laboratory had confirmed the preliminary tests and reports were published under its auspices, showing that the toxic ingredient was diethylene glycol. Maps were also published indicating the area in which the detail men of the Massengill Company had promoted the elixir to members of the medical profession. Recently an extensive report in *THE JOURNAL* by Geiling and Cannon¹ detailed the results of extensive studies of pharmacologic and pathologic effects following the ingestion of diethylene glycol or the Elixir of Sulfanilamide-Massengill.² During the first few weeks of the tragedy the United States Food and Drug Administration traced all shipments and removed them from the market. Federal inspectors also traced deaths reported in local communities. There was close cooperation between the government agencies and the headquarters of the American Medical Association. The publicity issued by *THE JOURNAL* warned the public; otherwise the number of deaths might have been higher. Had the medical profession followed the Council on Pharmacy and Chemistry, these tragedies would not have occurred: first, because the Council had consistently refused to accept, and to this day has not accepted, any liquid preparation of sulfanilamide, as there has been no evidence of usefulness and stability; second, because no product of the S. E. Massengill Company ever stood accepted for inclusion in New and Nonofficial Remedies. Had all physicians "followed the Council" or had the manufacturer followed the reasonable procedure³ of investigating the product before putting it on the market, nearly a hundred lives might have been saved. It will be recalled that the Secretary of Agriculture stated that the elixir had been prepared without any testing whatever other than that for flavor; that the total shipments amounted to 633. The number of deaths reported by government investigators as due to the "elixir" totaled close to a hundred.

The only basis of action under the Food and Drug Act, as pointed out by Secretary Wallace, was the

allegation that the word "elixir" implied an alcoholic solution, whereas the product was a diethylene glycol solution—notwithstanding the fact that there was evidence of danger from internal administration of diethylene glycol, prior to the marketing of Elixir of Sulfanilamide-Massengill.

To all such tragedies there is an aftermath. The unwarranted carelessness on the part of a pharmaceutical house awakened Congress and officials of the government to the necessity of taking action to protect the public. Congress passed a bill providing that no new drug or any modifications of old drugs may be placed on the market until the entire formula has been submitted to the Food and Drug Administration of the United States Department of Agriculture and the firm licensed to market the drug. Congress further enacted the long overdue Food and Drug Act, with somewhat awkward enforcement provisions. The Food and Drug Administration retains supervision over the product itself and over the labels and circulars accompanying the trade package. Claims made by other means, such as the radio, the spoken word, circular or newspaper advertising or even advertisements in medical periodicals (under certain definitions), are under the supervision of the Federal Trade Commission.

The Department of Justice, with the Food and Drug Administration, instituted legal proceedings against Samuel Evans Massengill, owner of the Massengill Company. A federal court at Greenville, Tenn., upheld the contention of the government that there was adulteration and misbranding. One hundred and sixty-six counts were filed against the concern, fifty-six charging that the drug was adulterated when it was shipped in that its purity fell below the professed standard under which it was sold and fifty-six charging that the drug was misbranded in that the name "Elixir of Sulfanilamide" was false and misleading. The remaining fifty-four counts charged that the drug was misbranded in that the statement "Quality Pharmaceuticals" appearing on the stickers attached to the corks of the bottles was false and misleading. The defendant, by his counsel, filed a demurrer to the charges. Following oral arguments and filing of briefs, the court ruled with the defendant with respect to the fifty-four misbranded counts involving the statement of "Quality Pharmaceuticals" but decided that the 112 counts alleging adulteration and misbranding in connection with the statement "Elixir of Sulfanilamide" did set up violations of the Food and Drug Act. October 3 the defendant's counsel pleaded guilty to the 112 counts of information and thereupon was sentenced to pay a fine of \$150 on each count, making a total of \$16,800. In addition there are still pending against Samuel Evans Massengill sixty-two counts to be brought before the district court of Kansas City, covering shipments of Elixir of Sulfanilamide made from the Kansas City plant of the company. Even if it might be assumed that the latter court will impose a similar fine for these counts, the

1. Geiling, E. M. K., and Cannon, P. R.: Pathologic Effects of Elixir of Sulfanilamide (Diethylene Glycol) Poisoning, *J. A. M. A.* **111**:926 (Sept. 3) 1938.

2. For details concerning the symptoms, examination of products and the many reports, see *THE JOURNAL A. M. A.* **108**:1340, 1345 (April 17), 1888 (May 29) 1937; **109**:358 (July 31), 1128 (Oct. 2), 1367 (Oct. 23), 1454, 1456 (Oct. 30), 1531, 1544 (Nov. 6), 1724, 1727 (Nov. 20), 1992 (Dec. 11) 1937; **110**:1610 (May 7) 1938; **111**:938 (Sept. 3) 1938.

3. See summary in article by Geiling and Cannon.¹

total would be \$26,100. The Food and Drug Administration merits commendation for its vigorous pursuit of the Massengill episode.

In the attempt to secure justice for the public in this case, federal officials were miserably handicapped by the weak law in existence at the time of the offense. A similar incident would not be dealt with so lightly under the new laws. Of course if the word "elixir" had not been used it is unlikely that any member of the medical profession would have prescribed the product, since "elixirs" are widely used and the solvents are not presumed to contain active or poisonous ingredients. Sulfanilamide itself has been recognized as an extremely valuable drug in restricted conditions. Physicians who used the elixir failed to realize that it is far safer to limit prescriptions of nonofficial articles to those brands accepted by the Council on Pharmacy and Chemistry and to use them as described in New and Nonofficial Remedies. It is always hazardous to prescribe unstandardized and uncontrolled remedies, or drugs sold under catchy names. Any pharmaceutical house which desires to market its products honestly and in accordance with the rules of the Council may have its products considered.

STAPHYLOCOCCIC FOOD POISONING

The continued frequency of outbreaks of poisoning due to staphylococcic contaminations of food serves to emphasize the importance of this condition as a public health problem. Special mention should be made of the outbreaks of food poisoning involving more than 250 men in the marine base at Quantico, Va., and of the 124 men on the U. S. S. *Arizona*,¹ of the 110 persons of twenty-eight families in San Francisco,² of the small outbreak that resulted from eating liver sausage in the Netherlands³ and of those reported in Hamilton, Ont.,⁴ and Billings, Mont.⁵ The Quantico and *Arizona* outbreaks were both attributed to contamination of ham with staphylococci, and that in San Francisco was attributed to custard cakes. In the Hamilton outbreak a number of strains of *Staphylococcus aureus* were isolated from cream and custard food products, from utensils and raw materials used in preparation of the food, and from the noses and throats of the employees in the bakery at which the food was prepared. The strains isolated could be divided into two distinct groups on the basis of their toxigenic and other properties. The data obtained leave little doubt as to the etiologic agent and the source of infection of the food; since the micro-organisms were so widely disseminated throughout the bakery it seems probable

that one person had spread the infection to his fellow employees and thence it was conveyed to the raw materials, utensils and finished food products. Similarly, the outbreak in Billings was attributed on investigation to filling for an orange cream cake, smears from which revealed staphylococci in large numbers. In this outbreak, however, investigations did not reveal the source of the contamination.

The symptoms of staphylococcic food poisoning are characteristic. The onset usually occurs rapidly following the ingestion of the infected material and is manifested by nausea, vomiting, abdominal pain, diarrhea and prostration without elevation of body temperature. While the symptoms vary in their acuteness, apparently depending on the toxigenic properties of the staphylococci involved, the train of events is characteristic and recovery is reasonably rapid and benign.

The symptoms described can usually be identified as food poisoning; the source can often be determined, but it has proved more difficult to ascertain the exact nature of the offending agent, since other organisms frequently cause similar symptoms. Furthermore, the determination of enterotoxigenicity has been fraught with great technical difficulties. Recently Dolman and his co-workers⁶ apparently devised a test for staphylococcus enterotoxin on kittens which appears to be both practical and specific. The enterotoxin has definite and specific antigenic properties and the serums of animals immunized with filtrates containing enterotoxin developed neutralizing properties against this antigen. A specific flocculation reaction can then be distinguished. This method has already received independent and confirmatory study.⁷ Other techniques for determining the toxic properties also are receiving investigation. Thus Chapman and his co-workers,⁸ in studying the food poisoning staphylococci, conclude that change in the cultural characteristics of these strains indicates degeneration, and hemolysis more than any other one quality appears to be the best indicator of degeneration. These investigators also studied the Stone reaction in a large number of strains. Stone⁹ in 1935 stated that strains of food poisoning could be differentiated from other staphylococci by their action on Stone's gelatin agar. Chapman and his colleagues found the Stone reaction positive in 70.5 per cent of typical food poisoning staphylococci and positive also in 27.6 per cent of strains with similar properties but isolated from non-food poisoning sources. They suggest, therefore, that the Stone reaction should be applied only to variants that react positively to the previously mentioned

6. Dolman, C. E., and Wilson, R. J.: Experiments with Staphylococcal Enterotoxin, *J. Immunology* 35: 13 (July) 1938.

7. Kirsch, C. L.: Some Cultural and Biochemical Characteristics of *Staphylococcus aureus*, *J. Infect. Dis.* 61: 320 (Nov.-Dec.) 1937.

8. Chapman, G. H., Lieb, C. W., and Curcio, Lillian G.: Isolation and Cultural Differentiation of Food-Poisoning Staphylococci, *Food Research* 2: 349 (No. 4) 1937.

9. Stone, R. V.: A Cultural Method for Classifying Staphylococci of the "Food Poisoning" Type, *Proc. Soc. Exper. Biol. & Med.* 32: 153 (Oct.) 1935.

1. Wade, E. M.: Observations on Staphylococcus Food Poisoning, *U. S. Nav. M. Bull.* 36: 306 (April) 1938.

2. Geiger, J. C.: Report of Two Outbreaks of Food Poisoning, *Pub. Health Rep.* 52: 765 (June 11) 1937.

3. Timmerman, W. A.: Voedselvergiftiging door Staphylococcen, *Nederl. tijdschr. v. geneesk.* 3: 443 (Sept. 18) 1937.

4. Wilson, R. J.: Laboratory Report of Strains of Staphylococci Isolated During the Outbreak, *Canad. Pub. Health J.* 29: 329 (July) 1938.

5. Cogswell, W. F.; Kilbourne, B. K., and Kuhns, Edith: Staphylococcal Food Poisoning in Billings, Mont., *Canad. Pub. Health J.* 29: 333 (July) 1938.

tests, since degenerate strains may be lacking in the Stone property. Whatever the result of this still controversial test, improved facilities for identification of food poisoning strains of staphylococci and their enterotoxic properties now seem imminent if not actually established. It must be remembered, however, that, in the words of Grubb,¹⁰ "the mere demonstration that bacteria isolated from foods implicated in food poisoning outbreaks are capable of producing a toxin is not incontrovertible evidence that these bacteria caused the outbreak."

Current Comment

INCIDENCE OF SYPHILIS AND GONORRHEA

In some tabular sheets¹ recently released by the United States Public Health Service the rates per thousand of population for syphilis and gonorrhea have been given by states and cities for the fiscal year 1938 and the month of July 1938. The highest annual rate for syphilis was reported from Florida with 14.19 per thousand, followed by Mississippi with 13.26 per thousand. The rate for gonorrhea in Florida, however, was only 1.76 but for Mississippi was 14.61. The total lack of parallelism exhibited between the rates for syphilis and gonorrhea in these two states alone (it was also evident in the figures from many other states) may be safely interpreted as indicating wholly unsatisfactory reporting of the latter disease. Similar discrepancies are evident in the figures for cities with a population of 200,000 or over and in the summary figures for July. If apparent increase in gonorrhea occurs this unsatisfactory reporting must be taken into consideration.

TOBACCO AND BLOOD PRESSURE

In an attempt to determine whether the change in blood pressure after smoking is due to the tobacco smoke or to other factors and whether the excessive rise in blood pressure occurs only in subjects who have a hyperreactive vascular system, Hines and Roth¹ have described the results of a standard smoking test. The subject is allowed to rest in a supine position in a quiet room for about thirty minutes or until the blood pressure and pulse rate reach a basal level. He then smokes two cigarettes of a standard brand and during the smoking and for a few minutes afterward the blood pressure and pulse rate are observed. In order to determine the role of mechanical and emotional factors a control test is made by having the subject go through the same procedure except that an unlighted cigarette is puffed. These tests were performed on fifty-six patients with essential hypertension and thirty subjects with normal blood pressure. All the normal subjects were smokers but eleven patients who had essential hypertension had not smoked prior to the test. There was a rise in either

systolic or diastolic blood pressures or both in most of the subjects tested, and the mean rise was of considerable amplitude. Response of blood pressure to the smoking test was similar to that to the cold pressor test except in the group of hyporeactors to the latter test. In the group of normal subjects only those who had an excessive response to the cold pressor test had an excessive response of the systolic and diastolic blood pressures to smoking. The mean rise in blood pressure was less in the control test, and in some instances there was even a fall in diastolic pressure. These observations were considered evidence that tobacco smoke was the main factor causing the rise in blood pressure but that excessive rises in blood pressure from smoking occurred only in the patients who had evidence of an inherently hyperreactive vascular system as measured by the cold pressor test. The effect of smoking tobacco on the blood pressure is apparently due not entirely to a nonspecific stimulus acting on a hyperreactive vascular system but at least in part to some element in the tobacco smoke which produces vasoconstriction.

INTERNATIONAL NUTRITIONAL PROBLEMS

Among the interesting discussions of the sixteenth International Physiology Congress, recently held at Zurich, was that on international problems of nutrition. The general status of the subject was reviewed by Profs. Emil Abderhalden of Halle and Gaetano Quagliariello of Naples. Harriet Chick of London pointed out that Europe and Asia have a relative sufficiency of energy-providing foods but that they lack protective foods, such as those containing vitamins and mineral requirements. She pleaded for studies to find some system whereby the present world imbalance in food supplies might be equalized. Magee of London suggested that economic factors are not the only ones concerned in providing a more equable distribution of foods. He emphasized that there are many racial peculiarities in food habits which determine the preference of certain peoples for certain types of foods. Later he deplored the application of experimental work in the laboratory to mass problems of human nutrition. By reference to India, he illustrated the difficulties of attempting to apply to an "underprivileged" race standards of nutrition devised under ideal experimental conditions. Leake from San Francisco then suggested that biochemists might examine the logic of their recommendations in nutrition. Size and weight, he believed, are not necessarily either the only or the best criteria of biologic excellence. What are called "optimum standards" are frequently taken from those amounts which in experimental animals produce maximum effects. Among many biologists there is a feeling that longevity is frequently curtailed by rapid and excessive growth. That American nutrition experts are becoming aware of some of these considerations is shown by the recent review of Simmonds.¹ International discussions such as this one are helpful in more satisfactorily coordinating general world opinion on the important problems of human nutrition.

10. Grubb, T. C.: The Present Status of the Staphylococcus Food Poisoning Problem, *J. Lab. & Clin. Med.* 23: 1150 (Aug.) 1935.

1. Public Health Service: Health Officers' Monthly Statement of Venereal Diseases Reported.

1. Hines, E. A., and Roth, Grace M.: The Effect of Tobacco on the Blood Pressure as Measured by a Standard Smoking Test, *Proc. Staff Meet., Mayo Clin.* 13: 524 (Aug. 17) 1938.

1. Simmonds, Nina: Nutritional Corrections as an Aid in Overcoming Growth Defects in the Oral Structures, *Internat. J. Orthodontia*, to be published.

ORGANIZATION SECTION

AMERICAN MEDICAL ASSOCIATION AND INTERDEPARTMENTAL COMMITTEES TO CONFER ON NATIONAL HEALTH PROGRAM

At the special session of the House of Delegates of the American Medical Association held in Chicago September 16 and 17, at which the National Health Program proposed by the Interdepartmental Committee to Coordinate Health and Welfare Activities was considered, the House of Delegates authorized the Speaker to appoint a committee to confer and consult with proper federal representatives with respect to that program. The committee appointed by the Speaker was as follows:

Dr. Irvin Abell, Chairman.	Dr. Frederic E. Sondern.
Dr. Walter F. Donaldson.	Dr. E. H. Cary.
Dr. Walter E. Vest.	and ex officio
Dr. Henry A. Luce.	Dr. Rock Sleyster.
Dr. Fred W. Rankin.	Dr. Olin West.

The Secretary of the Association addressed communications to the President of the United States and to Miss Josephine Roche, chairman of the Interdepartmental Committee to Coordinate Health and Welfare Activities, informing them of the appointment of this committee.

On October 12 a gracious letter was received from the President expressing gratification that the American Medical Association desires to be of service to the federal government "in connection with the development of sound plans for the betterment of public health and future expansion of medical service." The Presi-

dent's letter further indicated that he was pleased to learn of the action taken by the House of Delegates with respect to the National Health Program and indicated his belief that progress in translating the recommendations of the Interdepartmental Committee into a practical program undoubtedly can be made by conference with the Association's committee. It was further stated in the President's letter that he had referred the letter received from the Secretary of the Association and the report of the Proceedings of the House of Delegates to the chairman of the Interdepartmental Committee with the suggestion that arrangements should be made for a conference.

On October 10 an equally gracious letter was received from Miss Josephine Roche, chairman of the Interdepartmental Committee to Coordinate Health and Welfare Activities, indicating that the Interdepartmental Committee feels "that early discussions with the special committee of the House of Delegates will be of great value in the development of practical programs of action directed toward the improvement of public health and medical service." Miss Roche further indicated that the Interdepartmental Committee, including the Technical Committee on Medical Care, would like to have a conference with the committee appointed on authorization of the House of Delegates. This conference will be held in Washington on October 31.

AMERICAN MEDICAL ASSOCIATION STUDY OF MEDICAL CARE

Vanderburgh County, Indiana

Vanderburgh County covers an area of 233 square miles in the extreme southwestern portion of Indiana and is separated from Kentucky by the Ohio River. It had a population of 113,320 in 1930. Of the approximate 149,120 acres of land in Vanderburgh County, 81.9 per cent is in a rich agricultural district surrounding Evansville, which has a population of 102,249 and is the fourth city in size in the state. Evansville, founded in 1816 by General R. M. Evans, is a manufacturing and commercial city situated on a high bank of the Ohio River. The chief industries are the manufacture of flour, furniture and cigars. There is an extensive trade in coal, hardwood lumber and agricultural products, and within the vicinity of the city there are numerous coal mines.

The survey of Vanderburgh County was financed by a special assessment on the members of the county medical society and was supervised by a committee and directly conducted by a public accountant who was employed for four months. Each source of information was written in advance to inform it of the nature of the cooperation desired and was visited personally to interpret the various questions and insure uniformity in understanding and replying to the questions.

As a result of this preliminary action, 101 out of 134 physicians, or 75.37 per cent, and thirty-two of

sixty-one dentists, or 52.46 per cent, filled out and returned the questionnaires. The most remarkable returns were those received from other sources than physicians and dentists. Questionnaires were sent to four hospitals, four nursing associations, two health departments, thirteen welfare and relief agencies, fifty-nine schools, one college, 303 other organizations and eighty-two pharmacists; every one of these 468 questionnaires was returned with the requested information. The fact that only one out of nine questionnaires was sent to a physician and that the responses from other sources were 100 per cent offers the most complete answer to the sneering remark of a speaker at the recent National Health Conference, who said:

I do not myself feel much confidence in the result because I am not clear by precisely what method physicians are to know about the people whom they never see. The people who get no medical care obviously don't crowd the doctors' offices, and precisely how they are to arrive at figures which will be more convincing, if perchance we need any figures that are more convincing, is beyond the limits of my slow mind.

In considering reports of this survey one should keep in mind that information has been obtained from all organizations concerned in any significant way with medical care. Special efforts have been made to secure information from sources that might be supposed to have special information as to a lack of medical care

and might be disposed to criticize the attitude of the medical profession.

There are 134 physicians in active practice in Vanderburgh County, and no person is more than 8 miles from a physician. Nursing services are provided by 155 private duty nurses and twenty-three public health and visiting nurses. There are sixty-one dentists, eighty-two pharmacists and four hospitals. Of the latter, three are general and one is a hospital for tuberculosis; one is governmental, two are not for profit and one is private; these hospitals have a total of 582 beds, 145 of which are private and eighty-eight semiprivate, and 140 wards. There is a very exceptional condition as regards a quite uniform, high degree of occupancy in all types of hospital beds, the variation being only from 84.33 in semiprivate to 87.39 per cent of occupancy in wards. The ward rates vary from \$2 to \$3, and the private rates from \$4 to \$6.50.

Two clinics are operated by health departments and one is operated by "other organizations." One each of these clinics give the following types of service: maternity and child welfare, venereal diseases and dental. One private and twelve county (tax-supported) agencies arrange for or provide medical services. School health supervision services are under the control of the board of education and the Public Health Nursing Association. The one college in the county provides all types of medical service. There are seventeen plant arrangements for employees and eight for special groups of persons.

In 1937, 101 physicians who reported to the questionnaire stated that they had given free service during 1937 to 19,286 persons, and the thirty-two dentists who reported had given such service to 1,971 persons. In addition, 6,994 hours of service were given to the care of free ambulatory patients by physicians and 1,366 hours by dentists. The hospitals furnished 91,581 days of service to pay and part-pay patients, 15,795 to public charges and 40,860 days to free patients, while 9,777 patients made 18,276 visits to outpatient departments, clinics and dispensaries. Public nurses made 54,960 visits, of which 80.85 per cent were made without charge to the patients, and pharmacists compounded 20,216 prescriptions for which no charge was made and 5,850 at cost or reduced fees. Medicine for the indigent is provided principally by township trustees with the assistance of three small private societies. The ability of patients to pay for medical service is determined by investigation by hospitals and welfare and relief agencies.

With regard to hospital accommodations, the following comments are made:

We need twenty-five more hospital beds, especially for colored people. We have a ward, but no equipment as yet. This will probably be completed soon. What Evansville needs most is a general medical clinic. The tuberculosis clinic is oftentimes overcrowded because we have patients there who should not be there. Often patients who go there could go to a family doctor. As long as nurses make the selection this will continue.

Because of so high a percentage of bed occupancy, sixty-five patients needing hospital care in 1937 could not be admitted, but no person needing medical service was turned away from the outpatient department.

Some of the comments of the nurses were as follows:

Doctors do a good job in fulfilling their duty answering calls practically 100 per cent whether there is pay or not.

That in smaller cities, such as Evansville, where clinics and hospitals are not needed for medical teaching purposes, with

rare exceptions, no regular organized provision for adequate modern medical care is available to the underprivileged who are unable to purchase the service at the prevailing regulation rates. In consequence, many persons who are not at the moment suffering from an emergency type of illness must go without needed medical care. That what might be termed temporary emergency medical care is provided to indigents in Evansville through an older styled system of township trustee physician service. This service is a limited one. That some sort of modern set up is needed to provide necessary medical care for many adult citizens as well as children over the age of 6, who are ambulatory cases.

That the organized medical profession through progressive, cooperative leadership be the group to plan, devise and organize a modern agency to provide medical care to those in the community who cannot avail themselves of the needed service at the prevailing rates charged (which the private practitioner must charge if he is to exist) and at the prevailing rate of income of our large industrial population.

The total number of persons who were unable to obtain either medical, dental, nursing or hospital care is reported as eleven.

Of the 101 physicians from whom replies were received, sixty-eight stated that they had performed preventive medical services in private practice, thirty-seven said that they had done such work for health departments and twenty-seven that they had done such work for other agencies. Of course this includes some duplications, where physicians gave such service under all three conditions. No births were unattended by a physician or midwife, but 46.42 per cent of obstetric patients waited until after the third month of pregnancy before they consulted their physician. The county medical society has collected, as far as possible, from every organization having plans and arrangements for providing medical service or cash benefits for medical care material describing such arrangements but has not yet undertaken any specific plan of its own.

Further information contained in comments shows that \$16,560 was paid to doctors, \$43,027 to hospitals, \$18,048 for drugs, and \$30 for nurses, or a total of \$77,665, by the township trustees. In addition, the county department of public welfare expended \$9,266.

Among the recommendations by physicians, some of which are repeated several times, is the establishing of a free clinic for indigents to which physicians, in rotation, should give a certain amount of free service. Others suggest some form of hospital insurance or the building and maintaining of a joint county-city hospital. Another says: "We need our setup for x-ray and radium therapy of malignancy in the lower income groups," and another adds that there is need of "more extensive facilities for pneumonia-serum taking and serum available at a greatly reduced cost." Several declare, in substance, that all legitimate needs are now adequately taken care of or report that they have not heard any complaints. There is some complaint of politics and red tape and of a lack of organization; also, that "lodge practice, insurance and compensation work, mutual aid groups and similar organizations tend to encourage contract practice." It is probably a dentist who suggests "trailer traveling portable dental social service care with dental assistant aiding dentist." There are two who urge greater use of Negro physicians and Negro public health nurses in the care of the Negro sick. A full time health officer is suggested by several physicians, and one states that "I am of the opinion that the township and county physicians should be discontinued. The patient should be allowed to

choose the physician and the county should pay such physician a moderate fee." The following criticisms were also made:

Friends or relatives of indigents will not cooperate sufficiently to visit the necessary agencies to see about funds and services. Emergencies exist at all hours of the day and night and frequently it is impossible to serve authorization at these hours.

Frequently the methods are too complicated in order to insure indigent care. There is also frequently a lack of proper investigation; by this I mean indigent county patients all too frequently have new automobiles and all electrical appliances at home.

The medical association itself should work out some form of health insurance, to include doctor fees and hospital bills only, and present it to a reliable insurance company for sale to (1) the public who can buy it, (2) relief agencies supporting certain people, and (3) other governmental agencies. This insurance must not specify certain doctors or certain hospitals, but trust all certified and qualified M.D.'s the same.

These are but sample comments out of—as near as can be determined—some eighty to 100 comments or recommendations from physicians and dentists, which show the close interest and cooperation of the doctors in the study.

Especially significant to the medical profession are the comments from the welfare and relief agencies, because they represent an outside opinion; these are therefore given in full:

I feel that the doctors and hospitals here do a fine piece of work, and the care is adequate.

We feel that we should have a city hospital or additions to the hospitals already here. Some provision should be made for contagious and communicable diseases.

Better and more adequate care for colored patients.

Need an iron lung. Full time health officer.

I feel that care is adequate.

Doctors' fees are quite reasonable.

I believe the patient should pay back half the cost of his hospital bill or doctor bill after he gets back to work.

Hospital fees are too high. People would go to hospitals for necessities if the fees were more reasonable.

Doctors' fees should be lowered to a plane that the poor people could pay for and enjoy better health by receiving the care they need.

We need a city and county hospital combined that will also house all the clinics with full time doctors to take care of it.

I feel that the care is adequate, and the people are well served.

Lower rates are an absolute necessity and would do more good to solve the problem than anything else.

I feel that this city is large enough to support a city hospital.

I feel all welfare departments should be combined under one head.

The following comment from a school authority is helpful in outlining some phases of the local situation:

Reports continually come in from nurses, teachers, and social workers of children where parents are not able to provide medical and dental care for them. It is pointless and would be an unwise expenditure of effort unless there were some assurance of eventual attention to determine whether the reports are true or not. WPA wages and equally low incomes from industry, with a large number of dependents per family, is usually reasonable justification for assuming many reports to be true. A small amount of dental reparative work, a few tonsillectomies and refractions for outstandingly needful cases have been possible recently.

Several pharmacists suggest a clinic or additional hospital services, and one thinks that "indigent and low income groups should be taken care of through a good plan, with political aspects abolished, and turned over to medical society." There are a number of pharmacists whose opinions may be summed up in the statement of one of them that "doctors should be left alone to practice as they always have." Several others complain of political influence in the distribution of medical care to the indigent.

OFFICIAL NOTES

RADIO BROADCASTS

The fourth series of programs broadcast in dramatic form portraying fictitious but typical incidents of significance in relation to health by the American Medical Association and the National Broadcasting Company entitled "Your Health" began Wednesday, October 19, and will run consecutively for thirty-six weeks. The program is broadcast over the Blue network of the National Broadcasting Company each Wednesday at 2 p. m. eastern standard time (1 p. m. central standard time, 12 noon mountain time, 11 a. m. Pacific time).*

These programs are broadcast on what is known in radio as a sustaining basis; that is, the time is furnished gratis by the radio network and local stations and no revenue is derived

from the programs. Therefore, local stations may or may not take the program, at their discretion, except those stations which are owned and operated by the National Broadcasting Company. The programs to be broadcast in the first group, together with their dates and their topics, are as follows:

October 26. Growing Strong.[†]
November 2. Seeing and Hearing Well.
November 9. Healthier Boys and Girls.

* Owing to program conflicts, there will be no Chicago broadcast of the network program. Instead, a recording of the program will be broadcast over Station WENR at 8 p. m. each Wednesday. This recording will be an identical rebroadcast of the network program broadcast earlier the same day.

† Program may be canceled; attempting to arrange an evening program.

WOMAN'S AUXILIARY

Pennsylvania

The annual session of the auxiliary to the Medical Society of the State of Pennsylvania was held October 3-6 at Scranton.

Conferences were held with county presidents and chairmen of archives, history, Hygeia and public relations, with Mrs. Walter F. Donaldson, incoming president, presiding.

At the formal opening, October 4, Dr. Thomas G. Killeen, president, Lackawanna County Medical Society, gave an address of welcome. Following the business session, the annual luncheon was held with Mrs. David W. Thomas, second vice president

of the auxiliary to the American Medical Association, presiding. The speakers were Dr. Frederick J. Bishop, Dr. David W. Thomas, Dr. Walter F. Donaldson, Dr. Walter S. Brenholtz, and Dr. Frank C. Hammond.

At the afternoon session, Mrs. Augustus S. Kech gave an address on auxiliary work. A banquet honoring past state presidents was held at Hotel Casey. Dr. Howard C. Frontz, chairman, committee on Medical Benevolence of the Pennsylvania State Medical Society, reported to its house of delegates that the women's auxiliaries of Pennsylvania have contributed \$4,516.85 to the Benevolence Fund during the past twelve months.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

CALIFORNIA

Campaign Against Deafness.—California has been divided into eleven geographic areas with a district chairman, each of whom operates under a supervising state director, as an extension of the educational campaign to prevent impairments of hearing under way in the state for almost five years. Dr. Francis L. Rogers, Long Beach, is state director; Dr. Dewey R. Powell, Stockton, section chairman, and the following are the district chairmen:

Dr. Joseph Roy Jones, Sacramento, district 1.
Dr. Charles A. Broadus, Stockton, district 2.
Dr. Dorothea Lee, San Jose, district 3.
Dr. Harold A. Fletcher, San Francisco, district 4.
Dr. George W. Walker, Fresno, district 5.
Dr. Joseph D. Lewis, Santa Barbara, district 6.
Dr. Isaac H. Jones, Los Angeles, district 7.
Dr. Harold D. Smith, Pomona, district 8.
Dr. Ray M. Moose, San Bernardino, district 9.
Dr. Ben K. Parks, Long Beach, district 10.
Dr. Frank A. Burton, San Diego, district 11.

Society News.—The Los Angeles Cancer Society was addressed October 21 by Drs. Alson R. Kilgore, San Francisco, on breast tumors; William H. Sargent, Oakland, "Treatment of Superficial Cancer"; William H. Daniel, Los Angeles, "Surgery of Rectal Cancer"; and John H. Lawrence, Berkeley, "Neutrons and Artificial Radioactive Substances."—The first fall meeting of the Trudeau Society of Los Angeles will be addressed October 25 by Drs. James Steinberg, Maxwell T. Lipman and Julius L. Samuels, all of Los Angeles, and Joseph Rosenblatt, Duarte.—Dr. Arthur Elmer Belt, among others, addressed the Los Angeles Surgical Society October 14 on "New Approach Through the Perineum to the Posterior Aspect of the Prostate."—Henry Borsook, Ph.D., professor of biochemistry, California Institute of Technology, and Dr. Edward D. Krcmers, physician to students at the institute, presented a summary of the practical aspects of the vitamin situation before the Hollywood Academy of Medicine October 13.

CONNECTICUT

Public Health Meeting.—The Connecticut Public Health Association held a public health meeting September 21 at the Brady Memorial Auditorium, New Haven, with Dr. Wilmarth Bradford Walker, health officer of Cornwall, as the speaker. His subject was "How Towns Can Organize for Public Health." The meeting was open to the public.

Committee on Industrial Health.—Dr. Clifford Kuh, New Haven, has been appointed chairman of a recently created committee on industrial health of the Connecticut State Medical Society. Other members are Drs. William A. Sunderland, Danbury; Richard O'Brien Shea, Bridgeport; Benedict N. Whipple, Bristol; Donald B. Wells, Hartford; John Purney, New Britain; Paul W. Vestal, New Haven; John S. Dye, Waterbury; Cole B. Gibson, Meriden.

GEORGIA

Cancer Treatment Centers.—New state aid cancer treatment centers have been established at Dalton and Savannah, bringing the total number of these centers now in operation to ten. According to *Georgia's Health*, applications for state aid in the treatment of cancer are being received at about an average rate of seven a day.

Society News.—Dr. Wiley M. Flanagan, Waycross, addressed the Ware County Medical Society, Waycross, August 3, on the treatment of typhoid.—At a meeting of the Tri-County (Calhoun, Early and Miller counties) Medical Society August 18, the speakers were Drs. George O. Gunter, Blakely, on "Malaria, Prophylaxis and Treatment"; William H. Wall, Blakely, "Sulfanilamide, Its Uses and Abuses," and James A. Redfearn, Albany, heart disease.

Hall of Health for Atlanta Fair.—The Fulton County Medical Society sponsored a "Hall of Health" at the South-eastern Fair in Atlanta October 2-9. Contributors included the Medical Association of Georgia, the American Medical Association, the health departments of the state, Fulton County, and Atlanta, the Georgia and Atlanta tuberculosis associations, the fifth district dental, nursing and pharmaceutical societies,

the Atlanta Hospital Association and the Atlanta Dietetic Association. The Fulton County society displayed the work of famous physicians of Georgia, among other features.

ILLINOIS

Past Presidents' Night.—The Peoria City Medical Society held a dinner October 13 at the Pere Marquette Hotel in honor of its past presidents. Representative Everett Dirksen, as the principal speaker, discussed "The Present Day Status of Medicine in Congress." Twenty-seven former presidents of the society attended.

Chicago

Dr. Best to Address Institute of Medicine.—Dr. Charles H. Best, professor of physiology, University of Toronto Faculty of Medicine, Toronto, will address a joint meeting of the Institute of Medicine of Chicago and the Chicago Society of Internal Medicine at the Palmer House Friday evening at 8 o'clock, October 28, on "Heparin and Thrombosis."

Society News.—Speakers before the Chicago Laryngological and Otological Society October 3 were Drs. Thomas C. Galloway, Evanston, Ill., on "Postural Treatment in Acute Laryngotracheobronchitis"; Francis L. Lederer, "Early Diagnosis and Treatment of Laryngeal Carcinoma," and Joseph C. Beck, "Living Patients with Laryngectomies—Instruments for Otolaryngeal Diagnosis."

New Quarters for Social Hygiene Clinic.—Expanded facilities for the Municipal Social Hygiene Clinic are provided in new quarters to which the clinic has recently been moved. The first floor of the building remodeled for the purpose is for women, the second for men, with Dr. Cornelius E. Healy as chief clinician. On the third floor are laboratories for the clinic and facilities for outside activities, including epidemiology, physicians' reports, requisitions for drugs, follow-up and field work for other clinics. Laboratory work for private physicians and other clinics is done in the main laboratories of the city board of health.

Food Poisoning Attributed to Tainted Pastry.—About 500 cases of food poisoning with two deaths have occurred in Chicago and the suburb of Elmwood Park in an outbreak attributed to contaminated pastry from a bakery. Cases were first reported from Elmwood Park in newspapers of September 16. The Chicago board of health has investigated 121 cases within the city limits of Chicago and has found a history of eating pastry in about two thirds of them. The board of health of Elmwood Park and the state public health laboratory are investigating the cases in the suburb. The state laboratory announced September 21 that the paratyphoid bacillus was suspected of causing some of the cases, since the bacillus had been identified in several of the specimens. The Chicago department of health made a house to house canvass in the area of Chicago adjacent to Elmwood Park covering nearly three square miles, while the state and local departments of health cooperated in a similar survey in the suburb.

INDIANA

Graduate Education Meeting.—The Indiana State Medical Association, the Third District Medical Society and the Orange County Medical Society sponsored a graduate course at French Lick, September 7-8. The following program was presented:

Dr. Carl P. Huber, Chicago, Obstetrics in General Practice.
Dr. Alfred R. Shands Jr., Wilmington, Del., Common Clinical Orthopedics in Children.
Dr. Isidor H. Tumpcer, Chicago, Pediatric Adventures in Allergy.
Dr. Bernard Fantus, Chicago, The Role of the Spa in Therapy.
Dr. Richard Kovacs, New York, Use of Physical Therapy by the General Practitioner.
Dr. Walter S. McClellan, Saratoga Springs, N. Y., Recent Advances in the Therapeutic Application of Plain and Mineral Waters.
Dr. Madge C. L. McGuinness, New York, Physical Treatment in Gynecologic Conditions.

At the dinner meeting Wednesday evening the speakers were Drs. Emmet F. Horine and Arthur T. McCormack, both of Louisville, Ky., whose subjects were respectively "Prevention of Paroxysmal Dyspnea" and "Medical Practice and Public Health." Internal medicine and therapeutics and surgery and orthopedics were the subjects discussed at round table luncheons Thursday.

IOWA

Iowa Requires Citizenship of Foreign Graduates.—At a meeting of the state board of medical examiners in Des Moines September 9, a resolution was adopted requiring all applicants to practice medicine in Iowa coming from foreign medical colleges, exclusive of Canada, to furnish certified evidence that they have full citizenship in the United States.

Society News.—Dr. James B. Knipe, Armstrong, addressed the Emmet-Dickinson County Medical Societies August 18 in Estherville on spinal injuries.—The Wayne County Medical Society was addressed August 11 by Dr. Elias B. Howell, Ottumwa, on fractures.—At a meeting of the Des Moines Academy of Medicine and Polk County Medical Society in Des Moines September 27 the speakers were Drs. Henry G. Decker and Herman J. Smith on "Clinical Significance of Spinal Puncture" and "Coarctation of the Aorta" respectively.—Dr. James S. McLester, Birmingham, Ala., discussed "The Clinical Aspects of Nutritive Deficiency" before the Linn County Medical Society, Cedar Rapids, September 15.

LOUISIANA

Society News.—A joint scientific and third quarterly executive meeting of the Orleans Parish Medical Society was addressed October 10 by Drs. Oscar W. Bethea, New Orleans, on "The Analysis of the History in the Diagnosis of Gastric Disease" and Donovan C. Browne, New Orleans, "Gastroscoy."

Graduate Clinics.—The faculty of Tulane University of Louisiana School of Medicine, New Orleans, through the department of graduate medical studies, will present courses on medicine and surgery and their branches October 24-29. The mornings will be devoted to clinics and the afternoons to fifteen minute talks with five minutes between lectures for questions and answers.

MAINE

State Clinical Session.—The Maine Medical Association will hold its annual clinical session at the St. Mary's and Central Maine general hospitals, Lewiston, November 3-4. A dinner at the DeWitt Hotel Thursday evening will be addressed by Dr. Dennett L. Richardson, superintendent, Charles V. Chapin Hospital, Providence, R. I., whose subject will be "Contagious Disease Hospitals."

Society News.—Dr. Fred A. J. Geier, Washington, D. C., addressed a recent meeting of the Hancock County Medical Society, Bar Harbor, on "Criteria for Early Diagnosis of Cancer of the Stomach."—The Kennebec County Medical Association was addressed in Waterville September 15, among others, by Drs. Theodore E. Hardy on "Chronic Glomerular Nephritis" and Ovide F. Pomerleau, "Spinal Meningitis Treated with Sulfanilamide."—A recent meeting of the Somerset County Medical Society was addressed by Homer W. Smith, Sc.D., professor of physiology, New York University, on "Recent Studies in Renal Physiology."—Dr. Gilbert E. Haggart, Boston, discussed problems in bone and joint surgery before the Oxford County Medical Society in Bethel October 18.

MASSACHUSETTS

Personal.—A testimonial dinner was held in honor of Dr. Henry D. Chadwick, Boston, September 8; he has resigned as state health commissioner to become medical director of the Middlesex County Sanatorium at Waltham.

Cancer Clinic.—The regular Lawrence Cancer Clinic in Lawrence October 4 was a demonstration and teaching clinic for physicians with Dr. Channing C. Simmons, associate in surgery in courses for graduates, Harvard Medical School, Boston, as consultant. Physicians of the north half of Essex County were invited to bring their patients. A report is to be returned to every physician who sent a patient.

MICHIGAN

Physician Honored.—Dr. Amos S. Wheelock, Goodrich, an honorary member and past president of the Genesee County Medical Society, was honored by the people of Goodrich recently to observe his completion of fifty years of practice in the community. William J. Putnam gave the welcoming address; Judge Edward Black, Flint, was the principal speaker. Dr. Wheelock graduated at the University of Michigan Medical School, Ann Arbor, in 1888.

Rabies Committee Appointed.—A joint committee on the control of rabies in Michigan has been appointed to seek ways and means to curb the recent outbreak of rabies, which has caused two deaths. Members of the committee include Assistant Attorney General John F. Young; Dr. Filip C. Forsbeck, Lansing, director, bureau of epidemiology, state department of health; Dr. Herbert W. Emerson, director of the Pasteur Institute, Ann Arbor; C. H. Clark, state veterinarian, and Dr. Joseph A. Kasper, director of the laboratories of the Detroit health department. The committee represents the state department of health, the department of agriculture and the attorney general's office.

Graduate Course on the Specialties.—The department of graduate medicine of the University of Michigan Medical School, in conjunction with the Wayne University College of Medicine and the state medical society, announces the annual extramural graduate course for 1938-1939. The course has been divided into two parts, the first to be given in October 1938 and the second in April 1939. Surgery, dermatology, syphilology, internal medicine, including a symposium on tuberculosis, and psychiatry will be covered during the October session at the following teaching centers: Ann Arbor, Bar Harbor, Lake Michigan (jointly), Flint, Grand Rapids, Lansing, Jackson (jointly), Manistee- Traverse City-Cadillac-Petoskey (jointly), Marquette and Saginaw.

MINNESOTA

Personal.—Isaac M. Kolthoff, Ph.D., professor of analytic chemistry and head of the department of chemistry at the University of Minnesota, Minneapolis, was made an officer of the Order of Oranje-Nassau by Queen Wilhelmina of Holland August 31.—Dr. John Esser, Perham, has been appointed a member of the state board of health to succeed Dr. Samuel Z. Kerlan, Aitkin; Dr. Albert G. Schulze, St. Paul, has also been appointed a member.

Mayo Foundation House Dedicated.—The residence of Dr. and Mrs. William J. Mayo, Rochester, was dedicated September 23 "as a meeting place where men of medicine may exchange ideas for the good of mankind." The residence, now known as the Mayo Foundation House, and the east half of the block on which it stands was deeded about a year ago to the foundation together with sufficient endowment for its maintenance. The activities carried on there will be for medical education in its broadest sense and particularly with the view of fulfilling the purposes of the Mayo Foundation for Medical Education and Research.

Society News.—Dr. Philip Manson-Bahr, London School of Hygiene and Tropical Medicine, gave a Mayo Foundation lecture September 8 in Rochester on "Differential Diagnosis of Dysentery and Colitis."—Dr. Oscar F. Melby, Thief River Falls, was elected president of the Northern Minnesota Medical Association at its annual meeting in Crookston August 29-30. Dr. Charles W. Simson, Hawley, was elected vice president and Dr. Clarence Jacobson, Chisholm, reelected secretary and treasurer. Among the speakers were Drs. Ernest M. Hammes, St. Paul, on newer aspects of neurology and psychiatry, and Edward L. Tuohy, Duluth, on the present status of vitamin and hormone therapy.

MISSOURI

Annual Campaign Against Diphtheria.—The fourth annual campaign against diphtheria is under way in St. Louis under the auspices of the health division of the city department of public welfare. During the first eight months of 1939, before the first campaign, 584 children in St. Louis developed diphtheria and twenty-two of them died. During the first eight months of 1938 there were 128 cases and two deaths, representing a decrease of 78 per cent in the number of cases and 90 per cent in the number of deaths. Of the number of children who died in 1937 of diphtheria 94 per cent had not been immunized with toxoid or tested for immunity, it is reported.

The Ellis Fischel Cancer Hospital for Indigents.—Construction is expected to begin soon on the Ellis Fischel Cancer Hospital for Indigents in Columbia, which has been made possible through an appropriation of \$500,000. Later \$409,090 was granted the state cancer commission by the public works administration, making a total of \$909,090 for the construction and equipment of the hospital on a forty acre tract of land on highway 40 in Columbia, which gave the site to the cancer commission. The building will consist of seven stories and a penthouse, offering an approximate capacity of eighty-three beds. The hospital will be named for Dr. Ellis Fischel, who at the time of his death on May 14 was chairman of the state cancer commission.

NEW JERSEY

Society News.—Dr. Edward Weiss, Philadelphia, addressed the Camden County Medical Society, Camden, October 4, on "Recent Advances in Our Understanding of High Blood Pressure."—Dr. George A. Harrop, director of the Squibb Institute for Medical Research, New Brunswick, addressed a state meeting October 20 on "Recent Advances in Our Knowledge of the Adrenal Glands."—Dr. Edward J. G. Beardsley, Jersey City, addressed the Hudson County Medical Society, Jersey City, October 4, on "Clinical Demonstration of the Value of Routine Surgical Examination."

Fund Being Raised for Seashore House.—Funds for a new building for the Children's Seashore House at Atlantic City for Invalid Children are being raised by public subscription in Atlantic City, Philadelphia and surrounding communities. The new building will cost about \$1,250,000 and will have 420 beds. Wings will be especially constructed to allow wide areas of space for sun pavilions and a physical therapy department will be included in the new equipment to be added. An outdoor warm salt water pool will occupy the central foreground near the Boardwalk. Children's Seashore House receives convalescent, underprivileged and crippled children from hospitals and social agencies in New Jersey, Pennsylvania, Delaware and Maryland. Dr. Edward Z. Holt, Atlantic City, is medical director and Dr. Arthur Bruce Gill, Philadelphia, is head of the consulting medical staff.

NEW YORK

Personal.—Dr. Halsey J. Ball, health officer of the Utica district, including Herkimer, Madison and Oneida counties, retired from active service September 1, having reached the retirement age. He had been associated with public health work since 1892.

Typhoid in Resort Hotels.—Outbreaks of typhoid were reported in two resort hotels in upstate New York during the summer. In one case the drinking water from the hotel was taken from a well within ten feet of a sewer line. Examination of food handlers revealed that a waitress who had had typhoid as a child was harboring typhoid bacilli. She had begun work twelve days before the outbreak, in which twelve cases developed. In the second outbreak, the hotel cook was found to have had gallbladder attacks but had no knowledge of having had typhoid; the bacilli were found, however, on examination. Eleven cases occurred in this group.

District Meetings.—The annual meeting of the Fifth District Branch of the Medical Society of the State of New York was held in Syracuse October 6. A feature of the meeting was a luncheon in honor of Dr. William A. Groat, Syracuse, president of the state society, with Dr. Nathan B. Van Etten, New York, as the guest speaker. Among the speakers on the scientific program were Drs. Russell L. Haden, Cleveland, on "Mechanism of Anemia"; Herman O. Mosenthal, New York, "Protamine Zinc Insulin—Results of Its Prolonged Use" and Wendell D. George, Watertown, "Puerperal Infections, with Special Reference to the Use of Sulfanilamide."

—The Eighth District Branch of the Medical Society of the State of New York held its annual meeting October 4 at the Buffalo City Hospital. The guest speakers were Drs. Walter A. Bastedo, New York, on "Stomach Remedies New and Old" and William P. Murphy, Boston, "Fact and Fiction in the Treatment of Deficiency Diseases."

New York City

University News.—Richard E. Scammon, LL.D., distinguished service professor, Graduate School of the University of Minnesota, lectured before the New York University Chapter of Sigma Xi September 23 on "The Universalist Tendency in Seventeenth Century Science and Medicine as Exemplified by the Activities of the Versatile Dr. Petty."

Annual Dinner of Cancer Committee.—The New York City Cancer Committee will hold its annual dinner November 1 at the R. C. A. Building, Rockefeller Center, November 1. Dr. John C. A. Gerster, chairman of the committee, will preside; Dr. John J. Morton Jr., Rochester, N. Y., will present the greetings of the American Society for the Control of Cancer, and Mrs. Robert G. Mead, chairman of the society's committee on award, will present the Clement Cleveland Memorial Medal. The guests will then adjourn to the New York Museum of Science and Industry for a preview of the cancer exhibit prepared for the New York World's Fair. Addresses will be made by Louis I. Dublin, Ph.D., third vice president, New York Life Insurance Company; Mr. Robert P. Shaw, director, New York Museum of Science and Industry, and Dr. Francis Carter Wood, director of the Institute of Cancer Research, Columbia University.

Association of Allergy Clinics.—The first open meeting of the Association of Allergy Clinics of Greater New York will be held November 10 at New York University School of Medicine with "Hay Fever—Its Diagnosis and Treatment" as the subject of discussion. Allergy clinics of the following hospitals will participate: Bellevue Hospital, under the direction of Dr. Aaron Brown; the third pediatric division of Bellevue, Dr. Samuel D. Bell; New York Hospital, Dr. Horace S. Baldwin, and the New York Eye and Ear Infirmary,

Dr. James H. Barnard. This association was formed several months ago, and now has seventeen clinics as members. Only those have been accepted whose facilities, personnel and procedures had already been examined and approved as fulfilling the minimal requirements for allergy clinics established by the conjoint standards committee of the Society for the Study of Asthma and Allied Diseases and the Association for the Study of Allergy. Dr. Robert A. Cooke is chairman of the association and Dr. Robert Chobot is secretary.

NORTH CAROLINA

Services for Crippled Children.—The state board of health recently reported that about 12,000 children have been registered for examination, treatment or hospitalization by the crippled children's division since the division was established in April 1936, following the passage of the Social Security Act. Eighteen clinics have been organized, in many cases with support from local civic organizations. About 9,000 children have been admitted to these clinics for diagnosis or treatment. Arrangements were also made with eighteen general hospitals in the state, which provide about 100 beds in addition to the 150 beds at the State Orthopedic Hospital at Gastonia. During the two years the plan has been in operation there have been 1,784 cases authorized for admission to the general hospitals and 750 to the state orthopedic hospital. The field staff has attended 442 day clinics, resulting in contact with more than 7,000 patients. During the fiscal year ended June 30, the division expended \$216,000. This included \$114,000 state funds; \$96,000 from the Social Security Board through the Children's Bureau and \$6,000 contributed by civic and patriotic organizations.

OREGON

Society News.—The Lake County Medical Society was recently organized with Drs. Charles E. Leithead as president and Joycelin H. Robertson, secretary. Both are of Lakeview.

New Health Officers.—Dr. Peter H. Rozendal, formerly of Lake Preston, S. D., has been appointed health officer of Klamath County. Other recent appointments are Coos County, Dr. Charles L. Coyle, Marshfield; Multnomah County, Dr. Frederick Sydney Hansen, formerly of Pendleton, and Umatilla County, Dr. Alfred H. MacLaren, formerly of Portland.

PENNSYLVANIA

Negro Institute for Health Education.—A group of Negro physicians and dentists recently organized the Pennsylvania Institute of Negro Health under the leadership of Dr. Frederick M. Hopkins, Philadelphia, it is reported. Purposes of the organization are to disseminate health information among Negroes, to sponsor projects which will lead to the formation of health habits by Negro children and to interpret the aims of Negro physicians and dentists of the state, it was stated. Cooperation with city and county health departments and with the state department of health is planned.

SOUTH DAKOTA

Personal.—Dr. Antony Triolo, formerly of Philip, has been appointed health officer of Pennington County, succeeding Dr. Horace D. Lien, Rapid City, who has resigned to join the staff of the Fort Bidwell Hospital, Fort Bidwell, Calif.

TENNESSEE

Society News.—At a meeting of the Dyer, Lake and Crockett Counties Medical Society September 7 the speakers, all of Memphis, were Drs. James E. Wilson, on "Ophthalmology for the General Practitioner"; Sam L. Raines, "Management of Ureteral Stones" and Clyde V. Crosswell, "Suggestions for the Preschool Child."—Dr. Robert S. Cowles, Greeneville, addressed the Greene County Medical Society, Greeneville, September 6, on paratyphoid fever.—Drs. John B. Haskins and John Alexander Steward, Chattanooga, addressed the Hamilton County Medical Society, Chattanooga, September 15, on "Congenital Hypertrophic Stenosis in Infancy" and "Physiology and Surgery of the Sphincter" respectively.—At a meeting of the Shelby County Medical Society September 6, the speakers included Dr. Carrol C. Turner, Memphis, on "The Use of Metrazol in the Treatment of the Psychoses."—Dr. Walter D. Hankins, Johnson City, addressed the Washington County Medical Society, September 1, on "Roentgen Therapy in Infections and Malignant Diseases" and Dr. Edmund A. Lodge, Mountain Home, discussed cases of diseases of the eye, ear, nose and throat.

GENERAL

Hazards of the Hunting Season.—Analysis of 133 deaths in shooting accidents among hunters which occurred in industrial policyholders of the Metropolitan Life Insurance Company from 1935 to 1937 revealed three main groups of these fatalities, the *Statistical Bulletin* reports. Deaths resulting from self-inflicted wounds accounted for sixty, or 45 per cent, of the total number. Accidental shooting by a hunting companion was responsible for forty-eight, or 36 per cent. Nineteen persons were killed by hunters in other parties than their own; five were killed while resting by the accidental discharge of their guns set against rocks and trees, and one hunter was shot by a farmer who mistook him for a prowler. It is estimated that of nearly 3,000 persons killed each year in accidents with firearms about a third are hunters afield.

Premarital Blood Tests Required in Eight States.—Eight states now require premarital blood tests for both brides and bridegrooms before issuance of licenses to marry, according to a survey by the Council of State Governments reported in the *New York Times* October 3. New Hampshire became the eighth state October 1 when its law became effective. Other states are New Jersey, New York, Rhode Island, Connecticut, Illinois, Michigan and Wisconsin. Of the group, Rhode Island and Wisconsin are the only two with measures designed to prevent evasion of their laws. The Rhode Island law requires that residents married in other states who return to live in Rhode Island must, within six months, submit to physical examinations including blood tests. Residents of Oregon will decide in the November election whether its law shall apply to both men and women; at present only men are required to take premarital physical examinations.

Medical Care to Be Discussed in Newspaper Forum.—Care of the sick will be discussed in the eighth annual Forum on Current Problems sponsored by the *New York Herald Tribune* October 25-27. The discussion of medical care will be part of a session in the afternoon of October 25 on the general theme "Shall We Break with Tradition?" Robert A. Millikan, Ph.D., chairman of the executive council of California Institute of Technology, Pasadena, will deliver a keynote address and the following speakers will participate on the discussion:

Dr. Richard C. Cabot, professor of clinical medicine, emeritus, Harvard Medical School, Boston.
David McAlpin Pyle, New York, president of the United Hospital Fund.
Dr. Morris Fishbein, Chicago, Editor of *THE JOURNAL*.
W. C. Kirkpatrick, president of the Group Health Association, Washington, D. C.
Miss Josephine Roche, chairman of the Interdepartmental Committee to Coordinate Health and Welfare Activities, Washington, D. C.
Miss Esther Lape, member in charge of the American Foundation, New York.

This program will be broadcast over the facilities of the National Broadcasting Company.

Academy of Physical Medicine.—The sixteenth annual meeting and scientific session of the Academy of Physical Medicine will be held at the Willard Hotel, Washington, D. C., October 24-26. Among others, the following will speak:

Dr. Isi Guinzburg, Antwerp, Treatment of Hepatic Insufficiency by Physical Medicine.
Dr. Winfred Overholser, Washington, The Value of Physical Therapy in the Treatment of Mental Diseases.
Dr. Allen F. Voshell, Baltimore, Treatment of Poliomyelitis During the Postparalytic Stage.
Dr. Fred H. Albee, New York, Surgical Lengthening of the Top of the Femur in Anterior Poliomyelitis.
Dr. Josef B. Nylin, Philadelphia, Physical Exercise in Cardiac Conditions.
Dr. Benedict F. Boland, Boston, Lesions of the Uterine Cervix and Their Treatment by Electrosurgical Methods.

A public session Monday evening will be addressed, among others, by Dr. Rolland A. Case, Cleveland, president, on "Advances in Physical Medicine." At the round table luncheon Tuesday the theme will be "Electrical Brain Waves and Emotion in Man" with the following speakers: Hudson Hoagland, Ph.D., Dr. Donald Ewen Cameron and Morton A. Rubin, Ph.D., all of Worcester, Mass. The program also includes symposiums on radiant energy and fever therapy. Dr. Case will be master of ceremonies at the annual banquet Tuesday evening. In tribute to Dr. R. Tait McKenzie, who at the time of his death in April was the president of the Academy of Physical Medicine, an exhibit of rare bronzes, the work of Dr. McKenzie, will be shown.

International Congress of Military Medicine and Pharmacy.—The tenth International Congress of Military Medicine and Pharmacy will be held in Washington May 7-15, 1939, with Major General Charles R. Reynolds, surgeon general of the U. S. Army, as president. Registration is open to all officers of the medical services of the army, navy, air and

colonial services, national guard, territorial forces and public health service, both active and reserve. Subjects proposed for discussion are as follows: organization and function of the medical services in colonial expeditions, probable casualties in war and methods of calculation, practical procedures for anesthesia and analgesia in war surgery, organization and function of the military chemico-pharmaceutical service, emergency treatment and primary apparatus for fractures of the jaws in war, technical specialization of administrative officers in the medical service, and oxygen therapy and its practical use with troops on active service. Col. Harold W. Jones, Army Medical Corps, is secretary general of the congress, with headquarters at the Army Medical Library, Washington, D. C.

Delegates to Conference on Nomenclature.—Delegates from the United States to the International Commission for Decennial Revision of the International List of Causes of Death in Paris October 3-9 included the following:

William Thurber Fales, Sc.D., director, bureau of vital statistics, Baltimore Health Department.
Dr. William J. V. Deacon, director, bureau of vital statistics, Michigan State Department of Health, Lansing.
Mr. Thomas J. Duffield, director, bureau of vital statistics, New York City Department of Health.
Dr. Halbert L. Dunn, chief statistician, division of vital statistics, U. S. Bureau of the Census, Washington, D. C.
Sefwyn D. Collins, Ph.D., statistician, U. S. Public Health Service, Washington.
Dr. Edwin F. Daily, Children's Bureau, U. S. Department of Labor, Washington.
Dr. Haven Emerson, professor of public health practice, Columbia University College of Physicians and Surgeons, New York.
Mr. George H. Van Buren, general supervisor, Metropolitan Life Insurance Company, New York.
Dr. George Baehr, chairman, executive committee, Regional Conference of Nomenclature of Diseases, New York.
Miss Jessamine Whitney, statistician, National Tuberculosis Association, New York.

Government Services

Survey of Types of Cancer Treatment

The U. S. Public Health Service will undertake immediately a special study of the efficiency of various types of cancer treatment, it was announced October 3 at a meeting of the National Advisory Cancer Council. The council approved regulations drawn up by the National Cancer Institute for the loan of its grams of radium to various hospitals and clinics which are in need of radium for cancer treatment and for the skilled physicians and special equipment essential for its proper use. A feature of the meeting was the ground-breaking ceremonies for the new cancer institute on a fifteen acre site in Bethesda, Md. Mrs. Luke I. Wilson, who donated the tract, participated in the ceremonies. The \$600,000 building is expected to be ready for occupancy July 1, 1939. The next meeting of the council will be held Jan. 3, 1939, at which time it is expected several grants-in-aid to hospitals and research institutions will be awarded.

New Appointments in Public Health Service

The following have been commissioned as assistant surgeons in the regular corps of the U. S. Public Health Service:

Harold Martin Graning, Los Angeles
Vernam Terrell Davis Jr., Denver
Karl Habel, Philadelphia
Francis Theodore Zinn, Fort Worth, Texas
Ralph Erhart Wenzel, Mobile, Ala.
Robert Tedford Hewitt, New York.
Lawrence William Brown, San Francisco
Harold Tycho Castberg, Wenatchee, Wash.
Robert Roland Smith, Baltimore
Donald Roland Auten, Boston.
Murray Allen Diamond, Lexington, Ky.
Max Rudolph Kiesselbach, Los Angeles
James Allen Grider Jr., Angel Island, Calif.
Lamar Blewett Harper, Washington, D. C.
Franklin Lewis Price, Detroit
Weldon Algernon Williamson, Galveston, Texas
Robert Dean Wright, Washington, D. C.
Aaron William Christensen, Miami, Fla.
Carl Vincent Morrison, Springfield, Mo.

The following have been commissioned as assistant surgeons in the reserve corps for active duty at the places indicated:

Dr. Nobel W. Guthrie, U. S. Quarantine Station, Miami.
Dr. Robert McCune Jr., U. S. Public Health Service Dispensary, Washington, D. C.
Dr. Joseph H. Goldberger, U. S. Southwestern Reformatory, El Reno, Okla.

Foreign Letters

LONDON

(From Our Regular Correspondent)

Oct. 1, 1938.

Preparation for the Casualties of Air Raids

London has been described as "a province covered with houses." It contains over 8,000,000 persons. It was bombed on a small scale in the great war, and the danger of an attack on a larger scale has been foreseen and precautions have been taken. But no such gigantic problem, arising from the latest development of "civilized warfare," has been faced before. Air raid precautions, such as the manufacture by the government of gas masks for the whole population of the country, have been organized for some time. When the international tension became acute during the past week trenches were dug in the London parks and other open spaces, sections of the tube railways were closed to traffic so that they could be used as places of refuge and important buildings were sandbagged. Extensive plans for the evacuation of London were to be brought into operation on September 30 if the international tension was not relieved. Between 10 a. m. and 5 p. m., 500,000 school children and 2,000,000 other persons were to have been removed to a zone from 25 to 50 miles from London, in which billets and food supplies had been arranged. Never before in the world have mass movements been organized on such a scale. The evacuation was to be voluntary, but the billeting, for which preliminary surveys had been made, was to be compulsory. The evacuated persons would be given free railway tickets, but they would have no choice as to their destination. They were to take their gas masks with them. Nothing seems to have been neglected. Special precautions were even taken at the Zoological Gardens with regard to the animals. Basements in various parts of the gardens were strengthened with sandbags and equipped as air raid shelters. Supplies of sand were available at various points in case of fire. All poisonous snakes and spiders were to be killed immediately. Material was at hand for the immediate repair of cages, and should any large animals escape they were to be shot. The conversion of the motor coaches used for passenger traffic into ambulances, fitted with stretchers for the conveyance of the wounded, was arranged.

HOSPITAL ARRANGEMENTS

The arrangements for dealing with casualties were elaborate. Dressing stations for first aid were established all over London, for which lists of physicians were prepared. Physicians were to attend in shifts of eight hours so that two would always be on duty. At the hospitals, operating teams were organized and extra operating rooms fitted up. How complete the arrangements were may be shown by taking one hospital as an example, University College Hospital. Every one on the staff—physicians, surgeons and porters—and all the students were allotted duties. Twenty operating teams were organized, who were always to be on duty, day and night, in shifts of two. The hospital would thus be able to deal with 1,000 casualties from an air raid. The operating rooms were rendered gas proof. A complete transfusion service was organized. The admission of casualties to three destinations was arranged in every detail. There was to be a patrol of hospital porters, and crush barriers and a complete decontamination center were to be set up. Squads of students were on duty day and night making splints. A billeting officer was appointed who was to arrange for the housing of those on duty. There was a canteen staff for the feeding of everybody. Students were also appointed as stretcher bearers. The internal telephone of

the hospital was rendered bomb proof. A well known dermatologist was given the charge of all cases of burns. A special pathologic service was arranged. Even concert parties for the entertainment of both workers and patients were organized. The hospital records were stored in bomb-proof and gas-proof shelters.

These arrangements for dealing with 1,000 casualties from one air raid at one hospital show the numbers which were expected in London. That number could reasonably be multiplied by twenty for the whole metropolis. It was anticipated that 150 tons of high explosive might be rained down in one raid. Effectual precautions had been taken against gas and fire bombs, but against high explosives good protection could be afforded only by underground shelters, provision of which in any adequate number would have to be a matter of years. The official forecast was that air attacks on London would be severe for about a month and then rapidly fall off, as the anti-aircraft measures had been so perfected that the losses of the attacking force would be formidable and their numbers could not be kept up. Of course a good many civilians left London when the crisis became acute, but not sufficient to cause any apparent loss of numbers. The calmness with which the population faced the danger was remarkable. In most cases no difference of demeanor was evident after the danger was lifted.

A Modification of the Thomas Splint

It has been said of Thomas's splint that it is so perfect that all attempts to improve it have only had the opposite effect. Although it may not be possible to improve the splint as an appliance, modifications for the purpose of carriage or storage—problems which Thomas had never to face—may be possible. These problems have minimized its usefulness in the army, as has also the need of stocking various sizes. Mr. A. G. Ord has overcome the last-named disadvantage by an adjustable Thomas splint with an expandable ring. This when fully open will fit the largest thigh and when closed can readily be used as an arm splint. Bearing in mind these advantages, the medical directorate of the Indian army looked out for a more portable splint for frontier warfare than the standard Thomas splint. They found that Lieut.-Col. H. Horan Brown of the Indian medical service had devised a modification of Ord's splint which seemed to overcome all difficulties. Horan Brown has hinged the adjustable ring. On the outer surface he fitted a wing-nut, which firmly fixes or releases the hinge. The ring can be adjusted to any useful circumference and can be hinged to any comfortable shape to fit arm or leg. The splint can be packed when folded flat. This device means that in transport the Indian army is no longer compelled to tie its Thomas splint to a mule, camel or roof of an ambulance car but can pack a dozen or more in a fracture box. The design should prove of great value on account of economy in load and space for field medical units.

The Darwin Family

The Darwin family is a remarkable example of hereditary ability. The grandfather of Charles Darwin, Erasmus Darwin, was an early evolutionist, botanist and poet. Four of the five sons of Charles Darwin attained eminence as scientists. Sir George Darwin was a distinguished astronomer; Sir Francis was a botanist; Sir Horace was an engineer who provided the apparatus for the natural science laboratories at Cambridge. The only surviving son, Major Leonard Darwin, who is now 87, is well known as a eugenicist and economist. Dr. Charles Darwin, the son of Sir George and therefore the grandson of his great namesake, is professor of natural philosophy and Master of Christ's College, Cambridge. He is to preside next year over the Section of Mathematical and Physical Sciences of the British Association.

PARIS

(From Our Regular Correspondent)

Sept. 24, 1938.

Recovery from Streptococcic Empyema Following Chemotherapy

At the June 24 meeting of the Société médicale des hôpitaux of Paris, the twenty-first case of streptococcic empyema in France in which chemotherapy was employed was reported by Drs. Levy-Valensi, Sèze and Inbona. The patient was a woman, aged 59, with the typical physical signs of a large pleural effusion. Cultures made from the purulent fluid removed by aspiration revealed streptococci. The patient was given 2.25 Gm. daily of original prontosil. On the fifth day after the beginning of this treatment, 1,200 cc. of pus was aspirated, but only an occasional streptococcus was found in smears of the fluid. Five days later 700 cc. of pus was aspirated, but no streptococci could be found in the smears or cultures. The temperature dropped gradually, and x-ray examination of the chest three months after admission failed to show any fluid in the pleural cavity.

Septicemia with Meningitis Treated with Sulfanilamide

Drs. May and Mozzconacci reported at the July 8 meeting of the Société médicale des hôpitaux of Paris the case of a woman, aged 24, who was admitted to the hospital May 16, 1938, with symptoms of meningitis, which had appeared on the fifth day after an induced abortion. She was in stupor, with a high temperature and marked rigidity of the neck. Lumbar puncture revealed a turbid fluid containing many leukocytes and, on culture, a large number of streptococci. The blood culture was negative. The patient was given daily doses varying from 4 to 6 Gm. of sulfanilamide by mouth and on four successive days 0.85 Gm. intraspinally. In addition she was given 80 cc. daily of the Vincent antistreptococcus serum. Rapid improvement followed, so that the meningeal symptoms disappeared within three days and the spinal fluid inoculated on culture mediums failed to show any growth. However, the high temperature persisted and the blood culture became positive for streptococci on the fourth day after admission. The clinical signs of septicemia did not lessen nor did the blood cultures become negative, in spite of large doses, from 9 to 12 Gm., of sulfanilamide. Death took place about four weeks after admission. The interesting features were the complete recession of the symptoms of meningitis, accompanied by sterility of the spinal fluid, and the persistence of the generalized streptococcic sepsis despite a total dose of 181 Gm. of sulfanilamide. The authors expressed the opinion that if, in a case of streptococcic septicemia, the blood cultures continue to be positive chemotherapy has been of no avail and the prognosis is unfavorable. This patient had only slight cyanosis even when large doses of sulfanilamide were given.

Renal Nanism in a Rachitic Baby

The clinical pictures of renal nanism and of rachitis are familiar to pediatricians. De Toni in 1933 appears to have been the first to call attention to a third syndrome, in which, in addition to a combination of the symptoms and objective manifestations of renal nanism and of rachitis, there are disturbances of metabolism, especially of the glucides. De Toni considered this third syndrome the result of the coexistence of renal rachitis and renal diabetes with acidosis, the two dependent on the same cause. Since 1933 similar cases have been reported by other pediatricians. At the July 8 meeting of the Société médicale des hôpitaux of Paris, a typical case of the De Toni syndrome was reported by Dr. Marcel Lelong. An apparently normal female infant began at the age of 4½ months to have a loss of appetite and to show a cessation of growth. These manifestations were accompanied by evidences

of rachitis along the junction of the ribs and costal cartilages as well as by a temperature which went to 104 F. and a temperature curve showing marked oscillations. There was also an extreme degree of polydipsia. Careful search failed to reveal any connection between the persistently high temperature and a focus of infection or error in feeding. The signs of rachitis began, however, to be more marked during the following months, and these signs were accompanied by a noticeable retardation of growth and loss in weight. At the age of 11½ months, marked hepatomegaly was noted, as well as glycosuria, hyperglycemia after a tolerance test, hypercholesteremia, hyperlipemia, albuminuria with acidosis and a high blood urea content. These clinical and laboratory manifestations were accompanied by intense polydipsia. It is difficult to explain the persistent high temperature. The hepatomegaly and evidences of disturbances of metabolism were described as a "polycoric hepatomegaly syndrome" by Debré in 1931. The case reported by Dr. Lelong is the first in which the patient could be followed from the very onset of the De Toni syndrome. The x-ray appearances did not differ in any respect from those of typical rachitis.

Death of Professor Crouzon

The death of one of the leading neurologists of France, Prof. O. Crouzon, has been announced. After many years of effort he succeeded in convincing the other members of the faculty of the Paris Medical School that the field of social medicine had developed so rapidly that the subject should be included in the curriculum. Professor Crouzon was the first occupant of the newly created chair and began his course in the fall of 1937, aiming to include instruction on all types of social laws, many of which are in force here today. He was a commander of the Legion of Honor, attending physician at the Salpêtrière, the large Parisian hospital for neurologic disorders, and director of the school for nurses of the Paris public hospitals. A pupil of Dieulafoy, Babinski and Pierre Marie, Professor Crouzon was known all over the world through his contributions to neurology, especially on epilepsy, chorea and multiple sclerosis.

BERLIN

(From Our Regular Correspondent)

Sept. 10, 1938.

Biochemical Cancer Problems

Von Euler, professor of physiologic chemistry at Stockholm, recently lectured on biochemical cancer problems before the Berlin Medical Society. In present day oncologic research the metabolism of cancer cells occupies the foreground of interest. The author pointed out, among other things, that arginase is present in large quantities in cancers, that the increased nucleic acid metabolism leads to an increase in the peptidase value and that certain enzymatic changes appear in all the tissues as well as in the blood of patients with carcinoma. The author made particular reference also to the present status of the theory of carbohydrate decomposition, especially as to the effective mechanism of the enzyme system, set in action thereby. He reported the investigations carried on at his institute; these have led to the discovery of a new enzyme, diaphorase, which represents an important link in the chain of the dehydrogenation agent. In tumors an obvious displacement of the enzyme content is observable. For example, in sarcomas the ratio of dehydro-co-enzyme to co-enzyme is 6:10, as against 8:10 in the muscle. The cytochrome value is also lowered in sarcomas. Aerobic glycolysis of tumors, discovered by Warburg, according to the author is conditioned by a deficiency in the cytochrome system. The factors which can lead to the transformation of a normal cell to a cancer cell are manifold: predisposition, tarry substances, cancerigenic rays and so on. The problem of virus constitutes a special topic in itself.

According to the author, the virus of mosaic disease of the tobacco plant, which, as is known, can be isolated in crystalline form, obviously represents an enzyme complex. However, the problem of virus in human cancer remains unsolved. Cancer cells have frequently been said to originate in a mutation of normal cells. The author regards the cancer cell as a "cytochrome-deficient mutant," analogous to the well known mutation observed in plants; for example, the "chlorophyll-deficient barley mutants" produced by the irradiation of barley seed. Herein the author envisages a possible explanation of the *modus operandi* of cancerogenic rays.

The Roentgen Therapy of Myomas

The well known gynecologist and roentgen therapist Professor Gauss of Würzburg recently had published in *Strahlentherapie* a discussion of whether or not the almost complete rejection of surgical treatment, as practiced by him, in cases of myoma and preclimacteric metropathies, has been justified. Gauss employed irradiation in 955 (91.1 per cent) of 1,048 cases of these two conditions. On the basis of his experience he was able to formulate and verify the following guiding principles: 1. Radical treatment of myomas and preclimacteric metropathies is first indicated if the pathologic manifestations demand more than medication, baths and minor gynecologic therapeutics. 2. With preclimacteric metropathies it is only a question of irradiation. 3. Myomectomy is indicated only in certain infrequent circumstances: namely, if the tumor is of a pedunculated submucous nature, is pedunculated with a tendency to torsion of the pedicle or is subserous and already twisted about the pedicle; if the operation seems necessary to the maintenance of menstruation and fertility; if putrefaction or suppuration of the tumor, which could lead to general sepsis, is present, and, finally, if it is uncertain whether the neoplasm is a myoma or an ovarian tumor.

The German Roentgen Society

This year's congress of the German Roentgen Society, held at Munich, was considered the first Greater German convention of the society. The large number of Austrian delegates present participated as regular members.

The first theme for discussion was "Roentgenology and Public Health." A report was submitted by Dr. Blome of Berlin, a member of the staff of the national fuhrer of physicians. Notwithstanding the great difficulties entailed, an attempt must be made to encourage the utilization of roentgen procedures, even if on a small scale, by the general practitioner. With this in view, suitable miniature apparatus should be placed on the market. Present day conditions are certainly not propitious for a prompt realization of this aim, especially with regard to the roentgenologic training of the general practitioner. Dr. Blome perceives a need for separate departments of roentgenology, in which both medical students and graduate physicians may receive training. The study of roentgen procedures should be readily available; if this does not eventuate, instances of unskilful use of roentgen apparatus will continue to be encountered.

The second day's session was dedicated to therapeutics. It was marked by the reading of two papers on the treatment of cancer; Sauerbruch of Berlin discussed the problem as a surgeon, and Schinz of Zurich spoke as a roentgenologist. Both authors agreed that at present only two effective weapons against cancer are known: the knife and the ray. Among other things, Sauerbruch approved the exclusive use of roentgen therapy for tumors of the skin and of the accessible mucosa, even in cases of so-called "operable" cancer. Schinz described the cure in certain cases of cancer, including carcinoma of the vocal cords, by exclusive use of irradiation. On the basis of extensive verified statistics, Schinz attempted to prove the functional capability of irradiation in particular localizations of carcinoma. He then asked if surgery could

provide a corresponding array of incontestable statistics. The possibilities of roentgen therapy in the fight against cancer ought to be as completely developed as those of surgery, and on a similar independent basis. Then no longer, as at present, would a majority of patients be first submitted to roentgen therapy only after the disease has reached an advanced stage and, as often happens, after the failure of surgical measures.

A large number of individual reports were read to the congress, only a few of which can be mentioned here. Worthy of note were the data contributed by Schittenhelm, Munich clinician, on the indications for irradiation in the treatment of exophthalmic goiter and angina pectoris. In substance these observations represented verification of work previously done by French roentgenologists. The results reported by Chaoul of Berlin from his close radiation treatment of rectal carcinoma constitute a landmark in the advance of roentgen therapy and the expansion of its sphere of indication. In fourteen of twenty-three cases complete disappearance of the tumor was obtained. These favorable results are all the more noteworthy since the cases in question were of the inoperable variety of cancer. In addition to the favorable percentage of primary remission of symptoms, two of Chaoul's cases represent cures of four years' standing, with complete restoration of working capacity. Dyes of Würzburg reported roentgenologic cure of sarcomas, with no recurrence after five years.

ITALY

(From Our Regular Correspondent)

Sept. 15, 1938.

Crusade Against Mosquitoes

The general department of public health in Italy recently sent a circular letter to the municipal heads of public health, stating that the crusade against anopheles which has been carried on in the malarial zones has been successful. However, *Culex pipiens* is abundant in warm rural districts and balnearies. It is bothersome, though harmless. A campaign against mosquitoes in rural districts is to be carried on. Small agricultural centers will be inspected in order to prevent the formation of ponds and to control the sanitary conditions of water pipes and sewers. Wells will have to be covered and provided with pumps; horse ponds and public lavatories will be cleaned at regular intervals. The use of paris green alone is not sufficient to destroy *Culex* larvae in deposits of stagnant water which cannot be emptied. Oily liquids should be poured over the water and gambusia thrown in to spawn. For the actual destruction of mosquitoes, mechanical devices, pulverized liquid derivatives of petroleum and fumigation with pyrethric substances will be used. The campaign will be the most intense in nonmalarial zones and in climatic rest resorts.

Society Reunions

The Associazione Medica di Trieste recently met to discuss chemotherapy in the treatment of gonorrhea. Professor Levi reviewed theories on the mechanism of chemotherapy and reported his experiences with sulfanilamide. Sulfanilamide (streptosil) was administered to fifty of a group of 100 patients. The gonococcus disappeared from the secretions in seventeen cases during the first week and within three weeks, that is, four or five weeks after onset of the disease, in nineteen. Gonorrhea was controlled within forty-five days in the fifty patients who were given two or three cycles and lavages of sulfanilamide. Professor Freund administered dimethyl-disulfanilamide (uliron) to thirty-two patients with gonorrhea. Recovery was obtained in twenty-three cases. By further observation, the persistence of recovery was verified in fourteen cases. Nine of the patients did not return for consultation after the symptoms of the disease had disappeared. The treatment failed in seven cases. Two patients are still being treated. There were no accidents.

Professors Ravalico and Gentili administered one of three different sulfanilamide derivatives to each subgroup of a group of fifty-six patients who had gonorrhea. The treatment induced recovery in thirty-four cases and failed in twenty-two. Professor Robba administered different sulfanilamide preparations to eighty-two patients with gonorrhea. Original protosil (sulfamidochrysoidine) had a moderate antigonococcal action in eleven cases. The action of the drug was slower, less energetic and more toxic than that of some of the other preparations. The treatment is an adjuvant of the treatment in common use. Sulfanilamide was administered to forty-seven patients who had been suffering from gonorrhea for more than four weeks. It brought recovery in twenty-three cases within from eight to twenty days. Fifteen per cent of the patients, in whom the disease was of short duration, recovered. As a rule the patients received also local lavages with weak solutions of potassium permanganate. Sulfanilamide has an energetic antigonococcal action. As a result of his experience, the speaker is against prolonged administration of any sulfanilamide derivative and also against the use of the drug in the treatment of gonorrhea of short duration, as the drug may increase the resistance of the gonococcus. The speaker saw slight toxic effects in seven patients of a group of eighty-two who received the treatment.

AUSTRALIA

(From Our Regular Correspondent)

Aug. 17, 1938.

National Insurance in Australia

National insurance is now on the statute books in Australia in spite of the widespread opposition of the members of the medical profession. A royal commission, however, will report on the payment for and conditions of medical service and endeavor to make a recommendation which will be acceptable to those concerned. The members of the medical profession are not satisfied with the yearly fee of 11 shillings for the service expected of them, but the situation has been somewhat eased by the issue by Mr. J. B. Bridgen, commissioner of the National Health Insurance Commission, of a list of services which will be excluded from the scope of the National Health Insurance Act:

Care at confinement.

Service involving workers' compensation liability and similar insurance, for example the treatment of injuries incurred in motor accidents when claims for the cost of medical treatment can be discharged by compulsory third party motor insurance.

Administration of anesthetics necessitating the presence of a second practitioner.

Treatment of venereal diseases aside from advice as to the necessity of treatment and the infectivity of the condition.

X-ray investigation and treatment and radium treatment.

Pathologic investigations.

Massage.

Electrical diagnosis and treatment.

Consultations after full clinical investigation and adequate preliminary treatment.

Amputations.

Treatment of complicated fractures (such as a fracture penetrating a lung, a fractured pelvis penetrating the bladder or a fracture causing lesions of nerves and large blood vessels), compound fractures of the larger bones (excluding phalanges), fractures necessitating the skilled attention of an orthopedic surgeon (such as fractures of the femur), fractures necessitating an operation (including ununited fractures), fracture dislocations of the larger joints (excluding phalangeal joints) and dislocations of the spine or hip or any dislocation usually necessitating the skilled attention of an orthopedic surgeon.

Operations (1) involving the opening of a closed body cavity, such as the meninges, pleura, peritoneum or joint cavities; (2) involving organs not included in the preceding list, such as the uterus, kidney, ureter, bladder, urethra, eye and thyroid and (3) usually requiring the attendance of a specialist (including, for example, mastoid operations, dissection of the tonsils or nasal septum, sinus operations and operations for the treatment of malignant disease).

Treatment usually requiring the attendance of a specialist; for example, ophthalmologic treatment not ordinarily performed by general practitioners, treatment of special cutaneous diseases requiring the attendance of a dermatologist, specialized treatments of the more serious diseases of the bones and joints (such as tuberculosis requiring surgical treatment, osteomyelitis and suppurative arthritis) and specialist treatment necessitating the services of a neurologist or psychiatrist.

Medical Education

The high standards of medical education in Australia are generally recognized. In order to maintain these standards and to enable the medical profession to give efficient and faithful service, teaching needs should continually be under revision. Recent events in Melbourne, however, show that the university, through failure of public support, has not been able to fulfil its medical obligations. The recent occupant of the chair of anatomy (Prof. F. Wood-Jones), for lack of secretarial assistance, not only had been obliged to forego research but could not make that individual contact with his students which he regarded as one of the first obligations of a university teacher. While the various governments of Australia have poured students into the universities, they have shown either a complete disregard for or a lamentable ignorance of teaching requirements. The administrative authorities of the University of Sydney are confronted with the almost impossible task of providing for the training of physicians for the needs of the state with a laboratory accommodation and staff hardly sufficient for the needs of one-fifth the number of students who are entering the courses. There are nearly 300 students in the first year of medicine, and several of the other years are overcrowded. There is little possibility of making the personal contacts essential in medical education. Australian medical education is confronted with two kinds of disability: overcrowding of schools and inadequate staffing on the one hand, and scientific isolation of the individual schools on the other. Isolation from the scientific world and the distance of the universities from one another are serious handicaps to the spirit of cooperation found in smaller or more populated countries. Seldom, if ever, does the teaching staff of one Australian medical school come into such contact with the staff of another that its members know and appreciate the attainments and the work of their confrères from another state.

The Nutrition of the Australian People

Although there exist in Australia no gross food deficiencies such as are witnessed in the large industrial areas of America and England, recent investigations undertaken by the Commonwealth Advisory Council on Nutrition have provided widespread evidence of mild ill health produced by malnutrition. This council was appointed by the commonwealth government in 1936 after the League of Nations decision to investigate world-wide problems of nutrition. The final report of the council has been made available, and, although the results of the inquiry are not conclusive, they are very suggestive. The report shows that there is much ignorance in the community of the proper balance of food items and that some people in both town and country are unable to obtain the essential fresh foods. For these reasons a considerable mass of minor departures from normal health exist among children; up to 33 per cent of children examined were reported in an unsatisfactory condition. The evidence points to faulty selection of diets as the main cause of malnutrition, a selection sometimes necessitated by poverty but more often the result of ignorance. The ill health found is of two principal kinds: alterations in the growing bones resulting from lack of essential food elements, such as those contained in milk, fruit and vegetables, and alterations in the chemical balance of the body due to excessive intake of refined carbohydrates. Research proceeded along two main lines. First, an attempt was made to determine the nature and the quantity of food consumed by individuals, and, second, a clinical survey of children was conducted to determine their physical condition.

SURVEY OF HOUSEHOLD DIETARIES

The collection of data on diets presented some difficulty. An appeal through the press for cooperation by the public brought a poor response, and a system was finally instituted whereby housewives, reached mainly through baby health centers, recorded in a special book the details of all the food purchased for their families over a period of at least one month. The data thus received from 1,789 families can scarcely be considered a faithful representation of conditions actually obtaining in the community. The council admits that the data will show a position rather more fortunate than actually exists. Each of the 1,172 food items listed in the booklets was analyzed for its carbohydrate, fat, protein, moisture and ash content. Statistical analysis of the material showed that the weekly expenditure on food in the three eastern capitals varied between 11s. 6d. and 13 shillings for each adult male, while in Adelaide the figure was 10s. 2d. This discrepancy is due to the low utilization of milk and butter in Adelaide as well as to the home growing of fruit. Each adult male used 34 pounds of food a week, with a wastage allowance estimated at between 5 and 10 per cent. The caloric value of this average amount is more than sufficient to meet requirements. On a fuel basis alone however, although the average was high, 6 per cent of the diets studied were subliminal.

The consumption of protective foods fell far below an optimum allowance. Over 25 per cent of the dietaries studied showed inadequate consumption of milk, and 25 per cent failed to show a desirable consumption of eggs. The consumption of potatoes was below what is considered optimal. As to fresh fruit, 6 per cent of the adult males consumed half a pound a week and 12 per cent 1 pound a week. There was no evidence of an inadequate consumption of butter. No attempt was made to survey the vitamin content of the foods used.

CLINICAL EXAMINATION OF CHILDREN

The second portion of the investigation took the form of an extensive survey, conducted by Dr. F. W. Clements, of conditions in the far inland areas of Australia. Dr. Clements was equipped with an automobile unit consisting of motor caravan with sleeping quarters, small laboratory and portable x-ray unit. A physical examination determined whether the state of nutritional development of the child was "satisfactory" or "unsatisfactory." In addition, x-ray examinations of the epiphyses of the wrist, with blood and visual adaptation tests, were used to select the actual cases of malnourishment and to detect the actual effects of the malnutrition.

ECONOMIC FACTORS

A third section of the report gives consideration to economic and other factors involved in the consumption of protective foods. There is no shortage in the production of these foods in Australia, and the inquiry has clearly demonstrated that there is room for expansion of home markets. The council emphasizes the need for efficient distribution and proper storage of perishable foods in country districts.

RECOMMENDATIONS

In conclusion the council recommends as a guide for future action that the whole system of health supervision of children be immediately reviewed with the object of securing regular and complete supervision of bodily health during infancy and childhood to the age of 16 years and that regular instruction of all children in the elementary principles of hygiene and physical culture and of all girls in the composition and preparation of food be instituted. It is also recommended that a central coordinated committee be appointed to foster the general health of the rising generation, the correction of faulty diets in a general sense by the publication of dietary advice and the investigation and rectification of specialized local defects both physical

and nutritional. It has been suggested that a subcommittee of the National Health and Medical Research Council be formed to continue the function of the present Advisory Council on Nutrition, whose terms of reference have now been satisfied.

Cancer Investigation

Extensive plans have been made in Western Australia for a thorough investigation of a cancer treatment by the use of unorthodox biochemical therapies. The investigating committee has been appointed by the West Australian branch of the British Medical Association, and all expenses incurred will be borne by the state government. Dr. Koch, the discoverer of the treatment, which is asserted to have effected many cures in the United States, will probably be brought to Australia. In Australia little is known of Dr. Koch's work.

Marriages

ANDREW MATHEWS McLAUGHLIN, Waynesboro, Va., to Miss Betty Watkins Martin of Catawba Sanatorium, August 27.

ALLEN LEDYARD DE CAMP, Fayetteville, N. C., to Miss Katherine Besbord Bingham of Rydal, Pa., September 8.

LEONARD R. BOLOGNINO, Kew Gardens, N. Y., to Dr. CHRISTINE R. HEFFERMAN of Amsterdam, September 17.

EDWIN MACRAE RUCKER, Durham, N. C., to Miss Nancy Connelly Johnston of Nicholasville, Ky., July 9.

WILLIAM CHILDS CANTEY, Philadelphia, to Miss Blanche Mooror Dennis of Darlington, S. C., August 27.

ANDREW JOHN VALOIS KLEIN, East Orange, N. J., to Miss Louise W. Ripley at Point Pleasant, August 27.

CLARENCE C. CHEWNING JR., Bowling Green, Va., to Miss Alice Louise Thompson of Richmond, July 26.

ALLEN ARTHUR LILIENTHAL, Sanatorium, Miss., to Miss Jane Drexler Roth of Memphis, Tenn., September 4.

ROBERT S. ROSNER, Cleveland, to Miss Evelyn D. Harris of Monahans, Texas, at Cincinnati, September 4.

WILLIAM ROBERTS SANDUSKY, New York, to Miss Kate Wakeman Street of White Plains, July 4.

HENRY E. PALMER, Tallahassee, Fla., to Mrs. Leah Burgess Furlong of Rochester, N. Y., August 9.

IRWIN H. ZIELKE, Traverse City, Mich., to Miss Marie Elizabeth Cutler of Pittsburgh, July 28.

BERNARD S. STELMASZYK, LeRoy, N. Y., to Miss Irene P. Skarupinski of Buffalo, September 22.

HUGH GAMBEL CLARK, Fairfield, Ala., to Miss Buena Vista Gilchrist of Birmingham, August 16.

ROWLAND FRANKLIN ZEIGLER JR. to Miss Dickie C. Barfield, both of Florence, S. C., August 3.

WALTER GLENN HARDY, Roanoke, Va., to Miss Ethel D. Killinger of Rural Retreat, July 2.

ROBERT CLARK LAUGHLIN, Baltimore, to Miss Mary Alston Cowan of Blacksburg, Va., July 2.

LOUIS J. ZINTERHOFFER, Detroit, to Dr. MARTHA EFFIE MADSEN of Houston, Texas, July 25.

JOHN KIRK RICHARDSON to Miss Loula Clyde Woody, both of Richmond, Va., June 24.

CULLEN WARD IRISH to Miss Lois Patricia Heberling, both of Los Angeles, June 2.

ROBERT R. RUDOLPH to Miss Rachel M. Moore, both of Columbus, Ohio, July 2.

HENRY M. KARLAN, New York, to Miss Alexandria Stambler of Brooklyn, June 26.

VON A. LONG, Hartsville, S. C., to Miss Sara Elizabeth Ruff of Newberry, July 8.

LEWIS BETTY STATON to Miss Jeanette Bryce, both of Richmond, August 2.

JOHN H. LESIER to Miss Hilda Agee, both of Knoxville, Tenn., June 8.

HENRY M. LAMB, Portland, Maine, to Miss Helen B. Lord, August 24.

WILLIAM RICHARD McATEE, Erie, Pa., to Miss Sally Organ, August 24.

Deaths

Alexander Mason Evans, Baltimore; College of Physicians and Surgeons, Baltimore, 1912; associate professor of surgery at the University of Maryland School of Medicine; fellow of the American College of Surgeons and member of the Medical and Chirurgical Faculty of Maryland; served during the World War; aged 53; on the staff of the Mercy Hospital, where he died, July 24, of cardiovascular disease.

Harry Simpson Davidson, Akron, Ohio; Ohio Medical University, Columbus, 1897; member of the Ohio State Medical Association; past president and vice president of the Summit County Medical Society; at one time member of the board of education of Barberton; formerly member of the state legislature and county coroner; served during the World War; aged 67; died, August 1.

Charles Labram Vaux, Newark, N. Y.; University of Buffalo School of Medicine, 1902; member of the Medical Society of the State of New York and the American Psychiatric Association; served during the World War; aged 57; medical superintendent of the Newark State School, where he died in July of a skull fracture received in a fall down stairs.

Grace Elizabeth White, Ardmore, Pa.; Woman's Medical College of the New York Infirmary for Women and Children, New York, 1894; for many years physician in charge and owner of the Wood Lea Sanitarium; aged 69; died, July 5, in the Graduate Hospital of the University of Pennsylvania, Philadelphia, of carcinoma of the sigmoid and diabetes mellitus.

Haskell Talamo, Worcester, Mass.; Harvard University Medical School, Boston, 1926; member of the American Academy of Pediatrics and the New England Pediatric Society; on the staffs of the Memorial and Fairlawn hospitals, Worcester, and the Children's Hospital, Boston; aged 42; died, July 10, of subacute bacterial endocarditis and coronary embolism.

Clifton Rogers Dudley, St. Louis; Bellevue Hospital Medical College, New York, 1891; served during the World War; formerly medical director of the Missouri State Life Insurance Company and the Continental Life Insurance Company; aged 70; died, August 25, in the Veterans Administration Facility, Jefferson Barracks, of heart disease.

Harry Sebastian Reger, Jamestown, N. Y.; George Washington University School of Medicine, Washington, D. C., 1904; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; surgeon to the Jamestown Hospital; aged 60; was found dead, July 14, of coronary thrombosis.

John Vosburgh Stevens, Janesville, Wis.; Bennett College of Eclectic Medicine and Surgery, Chicago, 1885; at various times professor of pediatrics at his alma mater; an Affiliate Fellow of the American Medical Association; formerly member of the state board of medical examiners; aged 86; died, July 23, of pneumonia.

Amos Vastine Persing, Watsonstown, Pa.; Jefferson Medical College of Philadelphia, 1893; member of the board of health, and health officer for many years; at one time member of the board of education and bank president of Allenwood; aged 69; died, July 22, in Allenwood, of diabetes mellitus and pulmonary tuberculosis.

Frederick Berkley Bond, Southport, N. C.; University of Buffalo School of Medicine, 1906; member of the Medical Society of the State of North Carolina; served during the World War; aged 57; died, August 1, in the James Walker Memorial Hospital, Wilmington, of injuries received in an automobile accident.

John William Smith, Bronxville, N. Y.; University of the City of New York Medical Department, 1889; past president of the Westchester County Medical Society; at one time district health officer; aged 74; formerly on the staff of the Lawrence Hospital, where he died, July 2, of Parkinson's disease.

William Watson Wymore, San Francisco; Cooper Medical College, San Francisco, 1895; at one time served as police surgeon; on the staff of St. Francis Hospital; for many years member of the board of health; aged 72; died, July 29, of coronary occlusion and cirrhosis of the liver.

Anna Mabel Skinner, Watertown, Mass.; Boston University School of Medicine, 1903; member of the American Orthopsychiatric Association; associated with the Judge Baker Child Guidance Foundation; aged 71; died, July 24, of chronic nephritis, myocarditis and bronchopneumonia.

Henry Morris Spofford, Batavia, N. Y.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1902; veteran of the Spanish-American and World wars; formerly health officer; on the staff of St. Jerome's Hospital; aged 64; died, July 9, of heart disease.

James Glass, Framingham, Mass.; Harvard University Medical School, Boston, 1904; member of the Massachusetts Medical Society; served during the World War; formerly on the staff of Framingham Union Hospital; aged 67; died, July 4, of chronic myocarditis.

Emmott Howd, Troy, N. Y.; Albany (N. Y.) Medical College, 1898; fellow of American College of Surgeons; surgeon to the Leonard and Samaritan hospitals and obstetrician to St. Joseph Maternity Hospital; aged 66; died, July 9, of carcinoma of the stomach.

Harry Sydenham Van Etten, Stroudsburg, Pa.; Medico-Chirurgical College of Philadelphia, 1909; served during the World War; for many years secretary of the board of health; aged 55; died, July 14, in a local hospital following an operation for appendicitis.

Rose Harrison, Philadelphia; Woman's Medical College of Pennsylvania, Philadelphia, 1907; member of the Medical Society of the State of Pennsylvania; aged 54; died, July 20, in St. Agnes Hospital of perinephritic and nephritic abscesses.

Wilson S. Erdman, Quakertown, Pa.; Medico-Chirurgical College of Philadelphia, 1892; member of the Medical Society of the State of Pennsylvania; on the staff of the Quakertown Hospital; aged 70; died, July 17, of cirrhosis of the liver.

Martin Molony, San Francisco; National University of Ireland, 1888; member of the American Urological Association; fellow of the American College of Surgeons; aged 75; died, July 3, of chronic myocarditis and prostatitis.

Edward M. Scherer, Penn Yan, N. Y.; Bellevue Hospital Medical College, New York, 1893; member of the Medical Society of the State of New York; aged 68; died, July 19, in Rochester of arteriosclerosis.

Clifton A. Northrop, Hermon, N. Y.; College of Physicians and Surgeons, Baltimore, 1882; formerly health officer, and member of the school board; aged 82; died, July 12, of cerebral hemorrhage.

William Norwood Rogers, Trenton, N. J.; Hahnemann Medical College and Hospital of Philadelphia, 1898; served during the Spanish-American and World wars; aged 66; died, July 27.

Samuel Amos Stevens, Monroe, N. C.; University of Maryland School of Medicine, Baltimore, 1900; aged 67; died, July 9, in a hospital at Charlotte, of uremia and arteriosclerosis.

George Davis Farwell, Elmhurst, N. Y.; University of the City of New York Medical Department, 1888; aged 80; died, July 2, in the Pilgrim State Hospital, Brentwood.

Daniel Longaker, Reading, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1891; aged 68; died, July 22, in the Pennsylvania Hospital, Philadelphia.

Caroline Lee Danford Carson, Palo Alto, Calif.; Ohio Medical University, Columbus, 1898; veteran of the Spanish-American War; aged 68; died, July 4, of heart disease.

George Morley Muttart, Boston; University of Pennsylvania Department of Medicine, Philadelphia, 1890; aged 73; died in July of nephritis.

Lee Taliaferro, Madison Mills, Va.; University of Maryland School of Medicine, Baltimore, 1893; aged 72; died, July 19, of pneumonia.

Henry Griffen Salter, Cascade, Wis.; Wisconsin College of Physicians and Surgeons, Milwaukee, 1909; aged 56; died, July 11, of embolism.

Daniel J. Smith Jr., Elizabethton, Tenn.; University of Tennessee Medical Department, Nashville, 1894; aged 67; died, July 1, in Baltimore.

Lawrence Phillip Adamson, Girard, Kan.; University Medical College of Kansas City, 1894; aged 79; died, July 3, in Mount Shasta.

Charles Asa Hoag, Chicago; Chicago Homeopathic Medical College, 1891; aged 71; died, July 17, of organic heart disease.

Ellis Andrew Smith, Sunbury, Pa.; Baltimore Medical College, 1891; aged 70; died in July of uremia and nephritis.

William H. Keen, Nanton, Alta., Canada; Western University Faculty of Medicine, London, Ont., 1904; died, July 31.

Ralph Leonard, Berkeley, Calif.; Rush Medical College, Chicago, 1882; aged 86; died, July 25.

Correspondence

EVALUATION OF DRUGS USED AS DIAGNOSTIC AIDS

To the Editor:—In the interests of accuracy it should be pointed out that the recent review by Mettier and Leake on "Evaluation of Drugs Commonly Employed as Diagnostic Aids in Clinical Medicine" (*THE JOURNAL*, September 10, p. 986) contains statements which should be corrected in accordance with current technic. The most satisfactory compound for the rose bengal test of liver function is di-sodium-tetra-iodo-tetra-chlor-fluorescein and should be especially prepared for intravenous use. This is in accordance with the extensive experience of W. P. Stowe, G. D. Delprat and Alanson Weeks (*J. Lab. & Clin. Med.* 16:923 [June] 1931; and *J. Clin. Path.* 3:55 [Jan.] 1933; *J. Lab. & Clin. Med.* 20:1297 [Sept.] 1935). With regard to roentgenology of the urinary tract, a full historical survey appears in *Urological Roentgenology* by M. B. Wesson and H. E. Ruggles, Philadelphia, 1936.

C. D. LEAKE, PH.D., San Francisco.

Department of Pharmacology,
University of California.

THE SMALLEST BABY TO SURVIVE

To the Editor:—Some time ago Mrs. Grace Thomas of Le Sueur, Minn., read a statement that the smallest baby on record to live and develop normally weighed 1 pound 5 ounces (595 Gm.), which reminded her of the fact that she had a daughter who weighed only 20 ounces (567 Gm.) at birth. She asked me to forward her affidavit.

STATE OF MINNESOTA }
COUNTY OF LE SUEUR } ss.

Bridget Shea, being first duly sworn on oath deposes and says that she is over 65 years of age and that she lives at 402 North Second Street in the City of Le Sueur, Minnesota, and that she has lived at 402 North Second Street in the City of Le Sueur for over twenty years. Affiant states that Ruth Thomas of 316 North Second Street in the City of Le Sueur was born on February 24, 1920. Affiant was present at the birth of Ruth Thomas and she acted as mid-wife and helped Mrs. Grace Thomas, the mother of Ruth Thomas, bring Ruth Thomas into the world. Affiant states that Ruth Thomas was born at 7:30 A. M. Feb. 24, 1920, that affiant weighed the said Ruth Thomas the next day after her birth and that she weighed only twenty (20) ounces at that time. Affiant still has the scales on which affiant weighed the said Ruth Thomas, she still has possession of the scales and they are in working order, that the said Ruth Thomas was so small in size that she could almost lie in the ordinary retail cigar box, her fingers were not bigger than darning needles and her legs were no bigger than a lady's second finger. That Dr. Le Clerc was her mother's doctor at the birth of said Ruth Thomas, and Dr. Le Clerc at her birth said she would not live, she was so small. Doctor Le Clerc is dead and all the records are lost or destroyed. Said Ruth Thomas was so small in size that she attracted the attention of one thousand (1000) people who came to see her during the first few months after she was born. She was so small in size that she could not be dressed for two months after her birth, and that during first two months after her birth she could only be bathed with olive oil with the use of small applicators. Further affiant saith not except that she makes this affidavit for the purpose of stating and affirming that said Ruth Thomas weighed only twenty (20) ounces at birth.

Witnesses:

BRIDGET SHEA.

GERTRUDE OCHS.

FRED A. MCGUIRE

Subscribed and sworn to before me this 24th day of August 1938.

W. E. Ochs, Notary Public, Le Sueur County, Minn.

My Commission Expires April 8, 1944.

It is unfortunate that she waited so long to report this case, as in the meantime the attending doctor has died and all his records are destroyed. As I started practicing here in this town in 1922 I knew that the facts were reasonably accurate; but to verify the accuracy of the weight as closely as can be done at the present time, I interviewed the midwife, Mrs. Shea, now 82. Mrs. Shea is still alert mentally and active; when asked how she could recall the weight of the baby she said "I put the baby in a blanket and in a pan and put all on the scale, and it showed 2 pounds. Then I took the baby out and I weighed the pan and the blanket and that was three-quarters

pound, which left the baby's weight a pound and a quarter or 20 ounces." On being asked if she considered the scale accurate, she said she still had the same scale and brought it up. Checking with known weights showed it to be still accurate.

The mother brought in a small baby shoe, probably a doll shoe. I made an outline of the sole of that shoe on the back of the affidavit with the statement that the shoe was worn at 3 months of age. The mother also brought in a cigar box into which her husband tried to put the baby, stating that the legs had to be bent somewhat for the baby to lie in the box. Neighbors stated that at several different times they saw her in a shoe box.

Questioning both the mother and the midwife brought out that the labor apparently was extremely easy. There was practically no pain. The membranes ruptured while the mother was still up and around getting breakfast ready. The delivery took place within five or ten minutes thereafter, and the baby cried lustily at once and had a nice pink color. When the baby was 2 or 3 weeks old, some time in March, it had cyanosis and was revived by Mrs. Shea and developed normally without further mishaps.

At present Ruth Thomas is a very bright, intelligent, active girl, finished high school last spring and is entering college this fall.

SWAN ERICSON, M.D., Le Sueur, Minn.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

ACQUIRED OR CONGENITAL NEUROSYPHILIS

To the Editor:—A white man aged 29 complains of nervousness, loss of weight, a feeling of lassitude and insomnia of several months' duration. He is a clerk in one of the WPA divisions, is married and has two children aged 1 and 6 years, apparently in good health and normally developed. He had never undergone a physical examination. Physical examination revealed a typical Argyll Robertson pupil and absolute absence of the knee reflexes. The Romberg and coordination tests were negative. The blood examinations were Kolmer-Wassermann 4 plus, Kline 4 plus, Kahn 3 plus. The spinal fluid examination was Kolmer-Wassermann 4 plus, colloidal gold 123443221000, globulin no increase, cell count 65 cells per cubic millimeter. His history is entirely negative as regards a primary lesion or secondary manifestations. However, since this condition has been uncovered his mother states that years ago she and his father had syphilis, for which they had some treatment, probably not much. Is it possible that I am dealing with neurosyphilis of congenital origin? If so, what is the prognosis? What would be the best course of treatment to pursue in this case? M.D., West Virginia.

ANSWER.—The Argyll Robertson pupil and absent knee jerks (are the ankle jerks also absent and are there other signs of posterior column damage?), together with the character of the spinal fluid abnormalities, indicate definitely that the patient has tabes dorsalis. Much more important, however, the nervousness, loss of weight, lassitude and insomnia suggest that in addition to tabes dorsalis he also has dementia paralytica and that the correct diagnosis is the tabetic form of dementia paralytica. The serologic reactions are compatible with this diagnosis.

The presence or absence of stigmas of congenital syphilis are not mentioned. Unless such stigmas are definitely present, it is highly improbable, even though the patient's father and mother also had syphilis, that his disease is congenital and much more likely that it is acquired. The average age at the onset of juvenile dementia paralytica is 13 years and, as pointed out by Menninger in his monograph (*Juvenile Paresis*, Baltimore, Williams and Wilkins Company, 1936) it is extremely unusual for the initial symptoms of juvenile dementia paralytica to begin after the age of 25. Less than 1 per cent of 542 patients studied by Menninger had juvenile dementia paralytica after this age.

The differentiation between the congenital and the acquired form of the disease is, however, of the utmost importance from two points of view: First, as to the patient himself: The prognosis of the acquired form of dementia paralytica is, with proper treatment, much better than in juvenile dementia paraly-

tica, in which with any form of treatment the outlook is relatively hopeless. Second, from the standpoint of the patient's family: If the patient has the acquired form of the disease there is a strong possibility that his wife and both children are also infected. If, on the contrary, he has juvenile dementia paralytica the wife and children have certainly escaped.

In order to settle the issue between acquired and congenital syphilis, it is essential first to know whether the patient has any stigmas of congenital syphilis; second, to examine his brothers and sisters, if he has any, in order to determine their freedom from infection. His wife and children should also be examined. If they are infected, it may be assumed that the patient's infection is acquired.

The important feature of the prognosis is that related to the paretic component of the patient's illness rather than to the tabetic. If he is not properly treated, there is a strong probability that he will shortly become insane and that he will die within a few years from dementia paralytica, thus putting an entirely different face on the situation than the chronic invalidism which might result if his illness were purely *tabes dorsalis*.

The patient should certainly be treated immediately with artificial fever, preferably with induced malaria; a tertian strain should be used and the patient should be allowed to have at least twelve paroxysms of fever. On the completion of fever, and after a short course of small tonic doses of a trivalent arsenical, preferably neocarsphenamine or mapharsen, treatment should be continued for a minimum period of two years with tryparsamide and a bismuth compound as outlined in chapter XXVI of the monograph by J. E. Moore, *The Modern Treatment of Syphilis*, Springfield, Ill., Charles C. Thomas, 1933.

CONSTITUTIONAL PSYCHOPATHIC PERSONALITY

To the Editor:—A white man aged 23 is an adopted son and an only child. Nothing is known of his blood parentage, but the foster parents are cultured people and the home life has been ideal. The foster father is a lawyer. The patient had active tuberculosis in childhood, which cleared up after rest treatment was instituted. He became slow in his school work and because of this received a great deal of attention at home. Finally he finished high school and attended a junior college. Symptoms were first noticed at this boarding school. He became irresponsible; he lied but did not steal; he showed a lack of sustained interest; he wrote bad checks and signed his own name to them. He never mentioned this to his parents or to the bank on which he had drawn. His foster father usually took care of the checks but reprimanded the boy severely. He was given several jobs but did not hold any of them long. He was dismissed for being incompetent and inaccurate. He never worries in the least over not having a job. He contents himself by choosing undesirable companions and reading cheap literature. This certainly does not conform to the type of training and home life he has had. His foster parents are in moderate circumstances and are anxious to send him to school to complete his education. He has been referred to two neuropsychiatrists, both of whom called this a "borderline psychiatric case." I am not familiar with the term nor have I been able to find references to it. Can you give me references and indicate the prognosis of such a case? How should a case of this type be handled? Should the patient be reprovved for lying and punished for writing bad checks? He always has the most feasible story to explain any of his actions and never hesitates to explain them, although his stories are invariably false. He continues to ask his parents for money but never tells them where he is going or what he expects to do with the money. His parents have been exceptionally good to him, yet he tells strangers how mean his mother is to him and how he hates to go home at night because of the unpleasantness there. He resents any discipline from his parents or any one else. Any help you can offer will be appreciated.

M.D., Mississippi.

ANSWER:—Although the material supplied is rather scanty, the patient would seem to fit into the grouping of constitutional psychopathic personality. Under this heading are included people who have been from childhood or early youth habitually abnormal in their emotional reaction or in their general behavior but who do not reach, except perhaps episodically, a degree of abnormality which would justify calling them psychotic and who usually show no intellectual defect. Nothing is really known of the etiology of these conditions although the psycho-analytic school has stressed the fact that such individuals lack superego (conscience) and emphasize the fact that there is never a normal relationship between father and son in these cases. The treatment is exceedingly difficult and must of course vary for the individual. In general these people can occasionally be helped if they can form some sort of attachment to an older person who can advise them as difficulties arise.

The prognosis is usually bad. The subject may be found discussed in any standard textbook of psychiatry and the entire problem has recently been admirably reviewed by Dr. D. K. Henderson of Edinburgh at the recent Salmon Memorial Lecture at the New York Academy of Medicine. The volume is to appear soon and is a noteworthy contribution to a difficult problem.

DOSAGE OF GONAD STIMULATING HORMONES

To the Editor:—I am much interested in the use of anterior pituitary-like substance now so much in vogue in the treatment of nodoscent of the testis. As a urologist I have had the opportunity of operating in about 180 cases. Recently I have operated on a group of boys who have had varying doses of the anterior pituitary-like substance, and I think I have observed degenerative changes in some of the testes. This is in accord with the experimental work of T. W. Mimpriess published in the *Lancet* March 5, 1938. My own experimental work was undertaken before this date, but I killed my rats too early to show the changes which he noted. My second group is not yet ready for examination. The American literature is full of reports in which the recommended total dose varies from 1,000 rat units to 112,300 rat units. A discrepancy so great I believe is significant and somebody must be wrong. I expect to publish the results of my experimental work and should like to ask for an opinion as to the appropriate dosage. Digler has expressed the opinion that 4,000 rat units is the upper limit of safe dosage. The one case in which I have operated with this exact dose did not show gross degenerative changes.

J. S. EISENSTAEDT, M.D., Chicago.

ANSWER:—No standardized dosage (frequency and amount) of gonad stimulating agents (anterior pituitary-like) for clinical use has yet been adopted. It should be remembered that the total dose depends as well on the length of time administration is carried out as on the unitage employed for single injections. Since these water-soluble preparations are rapidly excreted, effectiveness of the preparation depends largely on the frequency of injection. Experiments on immature rats (from 15 to 35 days of age) with 100 units daily for a period of twenty days fails to cause degenerative changes in the testicle. Increased hormone production by the testes and increase in intertubular tissue is pronounced. Thompson and others (*Endocrinology* 22:59, 1938) report that doses equivalent to approximately 150 units daily over a month or longer in a 7 year old boy induced precocious maturity, a condition that should probably be avoided.

It is usually advisable to use moderate doses (from 300 to 500 rat units three times a week) and if the administration of these preparations has produced no favorable effect in a reasonable period, such as from six to eight weeks, continuation of the therapy is not indicated. This would avoid any possible danger which might exist from exceedingly high doses, but it must always be remembered that the present anterior pituitary-like products are chemically crude.

SONNE DYSENTERY IN TWO YEAR OLD

To the Editor:—A boy aged 2 has been troubled with loose, watery stools four or five times a day for the last three months. At no time has he been acutely ill. There has been no vomiting, loss of weight or apparent discomfort. He has remained alert and active with good appetite and a good disposition. The stools have contained a slight amount of mucus but no blood either grossly or by the benzidine test. The child is comfortable and well nourished and weighs 33 pounds (15 Kg.). No evidence of dehydration is present; the temperature and pulse are normal; no tenderness or masses are evident in the abdomen. Cultures of the stool reveal a *Sonne bacillus*. The urine is normal. Hemoglobin is between 80 and 90 and the red blood corpuscles number 4,220,000 per cubic millimeter. Various diets have been tried, the most recent being a low fat, low protein, high carbohydrate diet of low residue. The child has been given paregoric, calcium, belladonna and Kaomagma. As long as this treatment is continued, the diarrhea is controlled. Without medication the diarrhea continues. What suggestions can be offered for treatment? What is the value of colonic irrigation in this type of case? Of serum therapy?

M.D., Connecticut.

ANSWER:—It must be assumed that, if a *Sonne bacillus* was isolated from the stools of this child, it is a case of bacillary dysentery.

The most effective diet for a child suffering from liquid stools is one which consists of high proteins, low fats and a moderate carbohydrate intake, with an adequate supply of vitamins. Protein milk, skimmed milk or whole milk enriched with from 5 to 7.5 per cent of calcium caseinate should be included in the diet. Banana powder may be added to the milk mixture, and ripe bananas are sometimes taken with beneficial results. Later in the disease, cottage cheese, egg white, orange juice, a moderate quantity of raw apple, gelatin and lean scraped beef pan broiled may be given. Sometimes other vegetables may be added, though with great caution, and only one such substance should be added at a time. Bread or cereal should not be given until the diarrhea is under control. These patients have a low tolerance for carbohydrates and therefore sugars and sweets should be used sparingly. It is sometimes necessary to continue this diet in principle for a considerable time.

Serum therapy is effective only in cases of *Shiga bacillus* infection. The results of serum therapy in all other dysentery bacillus infections have been disappointing. The results with colonic irrigation also have been unsatisfactory, and as this procedure causes considerable discomfort and irritation it has come into general disuse.

TRAUMA AND VOLVULUS

To the Editor:—In a discussion of volvulus among several physicians, the question arose whether trauma might be a precipitating cause of intestinal obstruction. A case was mentioned of a watchman in his sixties who lifted a heavy weight and subsequently complained of abdominal pain and vomiting. These symptoms increased in severity, he became obstipated, and after two weeks he consulted his physician. Intestinal obstruction was diagnosed and at operation volvulus of the splenic flexure of the colon with thrombosis of the contributory vessels was found. Adhesions between other parts of the intestinal tract were seen. There was no history of previous operations. The available literature was of little help. Would you please enlighten me as to the relationship of trauma, or great strain as in the case mentioned, to volvulus?

M.D., New York.

ANSWER.—There is frequently a history of trauma or unusual physical activity in torsion of a solid viscus which is predisposed to it by a narrow pedicle or a bulbous round tip. Because these predisposing conditions may exist over a long period it is believed that initiation of the torsion is due to hyperemia of the veins mechanically favoring rotation around the tense arteries, which act as a mesentery and produce a spiral out of the convex side. A rubber tube will produce torsion under similar circumstances. These factors may occur in a distended appendix or any free loop of bowel, although torsion in the freely movable small intestine is rare except when associated with a Meckel's diverticulum, which may produce a volvulus by dragging on the bowel or by its increased weight when distended. Torsion of any viscus or loop of bowel is favored mechanically by fixation of both ends, so that it rotates around itself on two fixed points, similar to a folded handkerchief held taut by two corners while the third corner is allowed to rotate.

There is good evidence that an acute trauma from outside the abdomen or pressure from within may produce torsion of either a solid viscus or a loop of bowel. In torsion of a solid viscus the twisting mechanism is believed to result from an initial hyperemia with venous stasis due to trauma. Torsion of a loop of bowel is further favored by mechanical distention of a loop of intestine with gas, liquids or solid material, by increased peristalsis or by atony, which may rapidly predispose and initiate torsion. Since the latter factors may occur not only as a result of trauma but also in its absence as a cause of volvulus, it is either frequently overlooked or rarely occurs as contrasted with its recognized importance in torsion of a solid viscus. Regardless of its frequency as a cause of volvulus, trauma may produce all the factors necessary and should be a more frequent cause of volvulus than of torsion of a solid viscus where distention and peristalsis do not occur, but it is admitted that volvulus may result more frequently from nontraumatic factors.

As a rule volvulus rapidly produces obstruction of the bowel at both ends and complete strangulation of its blood supply with an early plastic peritonitis, which is followed by an infectious peritonitis from gangrene of the loop of bowel and death in a few days unless relieved by operation.

HAY FEVER FROM "COMPOSITE" POLLENS?

To the Editor:—What is the botanic name of the weed commonly known as "Spanish needle" or "beggar's lice"? This is a bright yellow flower growing profusely over the country. Is this plant capable of producing hay fever and if so, is a diagnostic and treatment set made by any of the biologic houses?

M.D., Illinois.

ANSWER.—While no one would dare give a definite answer as to the identity of a plant without a specimen of the plant in hand, it is quite likely that the plant referred to is one of the species of tickseed-sunflower, either *Bidens coronata* (L.) Britton, *Bidens trichosperma* (Michx.) or *Bidens involucrata* (Nutt.) Britton. These plants, variously known as beggar-ticks, beggar-lice, marsh marigold, bear wedge shaped achenes crowned with two short stout awns, whereas true Spanish needles (*Bidens bipinnata*, L.) bear spindle shaped achenes tipped with two, three or four barbed awns. The flowers of true Spanish needles are not conspicuous, often having no petals at all.

The pollen of this plant is capable of producing hay fever reactions and positive cutaneous reactions on persons sensitive to ragweed but one can get in contact with it only by direct handling of the plants. The pollen is heavy and suited only for insect transfer. There are no records of specific sensitivity to any member of the *Bidens* genus and no record of *Bidens* pollen ever having been found on atmospheric pollen slides exposed in any part of the United States. Pollen from this genus should not be regarded as of any more importance than that of any of the other composites. Britton states in his "Illustrated Flora of the United States and Canada" that there are 800 genera and not less than 10,000 species of the composites. This does not include members of the lettuce family, of which there are an additional 1,500 species. It is quite likely that the

pollen of any of these 11,500 plants would give positive reactions of varying degree on almost any ragweed sensitive person. Allergists agree that the active element in ragweed pollen is, as far as is known, shared by the pollen of all the composites. Furthermore, they generally agree that desensitization with ragweed pollen extract should protect a patient from any chance contact with small amounts of composite pollen. Only in rare cases in which a sensitized person is engaged in direct handling of unusual plants is it felt necessary to test with or include such pollens in desensitization treatment sets. Skin tests and pollen extract of *Bidens involucrata* can be obtained from Abbott Laboratories, North Chicago.

KÖHLER'S DISEASE IN ADULT OR ARTHRITIS

To the Editor:—A well nourished man aged 30, whose family history is negative, for the last five years has had pain in the right foot when he is on his feet. The left foot does not trouble him. Both feet appear flat in the longitudinal arch; there is slight adduction flexion and extension of foot normal range, but flexion is painful; adduction and abduction or eversion is zero and painful. X-ray examination shows irregular appearance of the dorsal surface of the anterior part of the astragalus and scaphoid and internal cuneiform. The scaphoid from the anterior view on both sides is narrowed and the astragalus scaphoid articulation shows denser outline of the scaphoid, suggesting Köhler's disease. Is this diagnosis right and what about Köhler's disease in adults? What is the treatment? C. C. RINARD, M.D., Homestead, Pa.

ANSWER.—Köhler's disease, first described in 1908, is seen only in children and adolescents. From the history and the x-ray appearances one would suspect an arthritic condition. A search for foci of infection should be made and syphilis must be ruled out.

Conservative measures are indicated, such as protection in sensible shoes with a good firm shank and heat to relieve pain. If there is swelling, the patient should sleep with the foot and leg elevated. Frequent enough x-ray examination is essential to determine whether there is any extension of the lesion. Fixation in a plaster cast is generally contraindicated in cases of this kind because of the resulting osteoporosis.

DANGERS FROM CHLORINATED DIPHENYL PREPARATION

To the Editor:—A patient has acute pericarditis with effusion associated with slight fever and leukocytosis. There is no cough and no sign of bronchial irritation. No cause can be found. The man has been working for five years as a special automobile mechanic for an oil company. One part of his work consists of using a substance called Solvenized Concentrate, made by the Dow Chemical Company, in the carburetor of the car. It is said to be a chlorine derivative of diphenyl. This substance is placed in the carburetor and the motor is allowed to run for some time. There is a great deal of smoke from the exhaust, to which the patient is constantly exposed. I do not see how it is possible for the inhalation of any gas to cause the trouble I have described, especially since there has been no bronchial irritation, but I would much appreciate an opinion on this and any information you might have on the possible poisoning from the substance described.

WILLIAM C. STEPHENSON JR., M.D., Roanoke, Va.

ANSWER.—It is unlikely that a chlorinated diphenyl preparation would cause the condition described. If nitrobenzene by mouth arbitrarily is associated with a toxicity rating of 1, diphenyl may be rated at 4 plus and 2-chlorodiphenyl at 2.5. These are the figures furnished by Smyth (The Toxicity of Certain Benzene Derivatives and Related Compounds, *J. Indust. Hyg.* 13:87 [March] 1931), who has carried out extensive experimental work with diphenyl and diphenyl derivatives. Drinker and his associates, in a symposium on certain chlorinated hydrocarbons, presented before the Harvard School of Public Health, Boston, June 30, 1937, reported extensive experiments with chlorinated diphenyls. In part, they concluded, "These experiments leave no doubt as to the possibility of systemic effects from the chlorinated naphthalenes and chlorinated diphenyl. . . . It is most remarkable too that all the compounds tested attack the liver and the liver alone. . . . On the basis of these experiments and on many field determinations of different compounds in the air of workrooms, it appears safe and it is certainly easily attained to ventilate so that the air breathed does not contain more than 0.5 mg. per cubic meter of any of these compounds above trichloronaphthalene." Reference to these two cited publications will furnish much additional information on the toxicity of chlorinated diphenyls. Even though no connection can be established in the present instance with a chlorinated diphenyl, the description of the operation furnished in the query suggests that this practice may be undesirable and that harm might arise. This patient, if only recently removed from exposure, should be examined to determine any disturbance in liver function. In many respects this form of intoxication resembles that from phosgene.

TREATMENT OF CHRONIC UNDULANT FEVER

To the Editor:—What is considered the most satisfactory treatment for chronic undulant fever with localized infection?

FRANK E. WIEDEMANN, M.D., Terre Haute, Ind.

ANSWER.—Several apparently satisfactory methods of treatment are now being employed in cases of chronic undulant fever (brucellosis). *Brucella melitensis* (abortus) vaccine (N. N. R.) appears to exert a favorable influence in a high proportion of cases. The response to vaccine therapy has been best in those patients who have experienced systemic febrile reactions following injections of the vaccine. In occasional refractory cases it may be necessary to increase the dosage beyond the 1 cc. which is usually regarded as a maximum dose.

Artificial fever therapy has been used successfully in the treatment of several cases of chronic undulant fever by Prickman, Burnett and Krusen (Treatment of Brucellosis by Physically Induced Hyperpyrexia, Proc. Staff Meet., Mayo Clin. 13:321 [May 25] 1938). Ervin and Hunt (The Diagnosis and Treatment of Undulant Fever, THE JOURNAL, Dec. 11, 1937, p. 1966) found that the production of sharp thermal reactions with intravenous injections of typhoid-paratyphoid vaccine usually shortened the course of the disease.

Successful results have been reported following the use of a broth filtrate of *Brucella* organisms, known as "brucellin," developed by I. F. Huddleson, Michigan State College, East Lansing, Mich. More recently, Stern and Blake (Undulant Fever: Its Treatment with Sulfanilamide, THE JOURNAL, May 7, 1938, p. 1550) and Blumgart (Recovery of a Patient with Undulant Fever Treated with Sulfanilamide, THE JOURNAL, Aug. 6, 1938, p. 521) have used sulfanilamide in the treatment of a few patients with acute or subacute undulant fever, with apparently prompt and favorable results.

IRITIS FROM SCISSORS

To the Editor:—Six weeks ago a girl aged 17 years had a perforating wound of the cornea just below the pupil, having jabbed the point of a pair of scissors into the eye while sewing. There appeared to be little or no damage to the iris and the lens; the eyeball was somewhat softened. Treatment has consisted of the use of White's ointment and a firm bandage. The eye seemed to do well and the sight has steadily improved, but on the last visit the sclera seemed somewhat more congested than it had recently been and the eyeball appeared to be just a little smaller than the other. There has at no time been any great amount of exudate in the anterior chamber, nor has there been any excessive amount of pain. What are the chances of atrophy of the eyeball and loss of sight? What are the chances of sympathetic ophthalmia?

M.D., West Virginia.

ANSWER.—A simple perforating injury of the cornea without subsequent purulent infection of the eyeball and without traumatic iritis never leads to an atrophy of the eyeball or phthisis bulbi. However, from the description, it appears that there is an iritis, probably increasing in amount, judged by the evident thickening of the lids and decreased palpebral aperture and by the increased ciliary hyperemia. Consequently there must have been some injury to the iris and as a result there is a definite danger of sympathetic ophthalmia. More active treatment is indicated in the form of complete atropinization, use of sodium salicylate and foreign proteins.

FORMALDEHYDE DISINFECTION OF SHOES

To the Editor:—I was much interested in the article "Removing Formaldehyde from Leather," in the July 30 issue of THE JOURNAL. Formaldehyde is recommended for disinfecting shoes in cases of ringworm. The author failed to state what method should be used to eliminate objectionable features of formaldehyde. I used this drug in my own case last week, putting on my shoes the next morning and as a result suffered severe burns and deep fissures on the soles and between the toes. 1. What is the best method to disinfect shoes? 2. Is roentgen therapy a good method for treatment of ringworm of the feet, and what is the usual dosage and frequency of application? 3. Can the formaldehyde be neutralized in shoes sufficiently to prevent harm to feet? How? 4. What is the treatment for fissures resulting from formaldehyde?

M.D., Ohio.

ANSWER.—Formaldehyde for disinfecting the shoes in fungous infections has been widely used and generally approved. It is necessary that the shoes be thoroughly aired after exposing them to the action of this agent. A two day interval after application generally proves satisfactory. Probably this interval could be considerably shortened if a stream of air was blown through the shoes or if a fan was placed in front of them.

1. This remains an open problem, but it is probable that the chemical method is as practical as any.

2. X-rays are frequently used by dermatologists for treating eczematoid ringworm of the feet, but their use should be limited to those thoroughly acquainted with this modality.

3. The most practical way of getting formaldehyde off the shoes is by evaporating by exposure of the shoes to the air.

4. If the dermatitis and fissures resulting from the use of formaldehyde are severe, wet dressings of aluminum subacetate solution 0.5 per cent may be used early. When the acuity of the disorder subsides, boric acid ointment or similar bland material may succeed this. After the condition becomes stationary, the use of a modified Whitfield ointment may be cautiously begun. This would consist of about 1 to 2 per cent salicylic acid and 2 to 3 per cent benzoic acid in petrolatum. The concentration of these ingredients may be increased as the process warrants.

DEXTROSE TOLERANCE TEST

To the Editor:—A white woman aged 57, known to be diabetic for ten years, who one month previously had been in diabetic coma, had at the time of a dextrose tolerance test an active right pyelitis. A dextrose tolerance test was given, 100 Gm. of dextrose being administered by mouth. The following blood sugar determinations were obtained: fasting, 400 mg per hundred cubic centimeters; one hour, 575 mg.; two hours, 660 mg.; three hours, 735 mg.; four hours, 675 mg. The patient at the time of the test was taking 80 units of insulin daily. Was this not a dangerous and unnecessary test to perform in such a patient? M.D., Arkansas.

ANSWER.—It was not a dangerous test to perform because undoubtedly the patient was taking 100 Gm. of carbohydrate daily and it simply meant that she was given the 100 Gm. in a short time. Often after operations one gives 1,000 cc. of physiologic solution of sodium chloride intravenously with from 50 to 100 Gm. of dextrose even though the blood sugar may be temporarily high. Such an injection might be postponed until the blood sugar drops, but one usually prefers to permit transient hyperglycemia rather than to have the patient go twelve or even twenty-four hours subsequent to operation without carbohydrate. By the use of insulin at frequent intervals the hyperglycemia can be easily controlled.

Whether it was unnecessary to give the dextrose tolerance test, as one might be tempted to conclude, would be improper to say without knowing all the circumstances which the doctor had in mind at the time he gave the test.

PNEUMOTHORAX REFILLS IN EUROPE

To the Editor:—A patient who has been having pneumothorax treatments for tuberculosis for the last two and a half years is now having a refill every three weeks. She wishes to take a trip abroad and wants to know where refills can be obtained in France, Germany, Austria, Switzerland and Italy.

M.D., Illinois.

ANSWER.—There will be no difficulty in receiving artificial pneumothorax treatments while abroad. Excellent collapse therapy work is done in all the places mentioned. The following physicians are well qualified:

In France, Dr. Edouard Rist, médecin des hôpitaux de Paris, 5 rue de Magdebourg, Paris, 16^e; in Germany, Dr. Walter Unverricht, Leiter der III med. Univ. Poliklinik, Kaiserallee 23, Wilmersdorf, Berlin; in Austria, Dr. Ludwig Hofbauer, Leiter der Atmungspathologischen Abteilung, I. Medizinischen Klinik, Vienna; in Italy, Dr. Federico Bocchetti, Direttore del Sanatorio Bernardino Ramazzini de Roma, Via Nazionale, 22, Rome; in Switzerland, Dr. E. Bachmann, Kirchgasse 36, Zurich 1, or Dr. Marc Jaquero, directeur du Sanatorium du Grand Hotel, Leysin (Ct. de Vaud).

VARICOSITIES OF LIPS AND FACE

To the Editor:—I have been consulted by a middle aged man about a small varicosity protruding downward about 3 mm. from the mucosa of the upper lip; it is approximately 8 mm. in diameter. What success can I anticipate in the obliteration of this mass by the perivenous injection of small amounts of a mild sclerosing fluid, such as sodium psyllate fluid?

M.D., Missouri.

ANSWER.—Small vascular dilatations on the lips may readily respond to an injection of a few drops of some mild sclerosing solution into the mass but not around it. A traumatic etiology is likely. One should always look for vascular masses below the buccal mucous membrane, in the substance of the upper lip, in the cheeks or in the bony structures, as often a large vascular anomaly may be hidden behind an innocuous, cutaneous varicose. If vascular nevi are present in other regions of the face, the suspicion of a congenital vascular anomaly may be aroused. Certain slowly growing malignant neoplasms may produce venous compression and manifest themselves in an early venous engorgement. If radium is available, it will shrink the vascular mass effectively.

Medical Examinations and Licensure

COMING EXAMINATIONS

STATE AND TERRITORIAL BOARDS

Examinations of state and territorial boards were published in *The Journal*, October 15, page 1495.

SPECIAL BOARDS

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY: *Oral*. St. Louis, Nov. 11-12. Sec., Dr. C. Guy Lane, 416 Marlboro St., Boston.

AMERICAN BOARD OF INTERNAL MEDICINE: Written examinations will be held in various parts of the United States, Feb. 20. Application must be received on or before Jan. 1. Sec., Dr. William S. Middleton, 1301 University Ave., Madison, Wis.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: Written examination and review of case histories of Group B applicants will be held in various cities of the United States and Canada, Nov. 5 and Feb. 4. General oral, clinical and pathological examinations for all candidates (Groups A and B) will be given in St. Louis, May 15-16. Applications must be filed not later than sixty days prior to date of examination. Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh (6).

AMERICAN BOARD OF OPHTHALMOLOGY: St. Louis, May 15. Applications must be filed before February 15. Sec., Dr. John Green, 3720 Washington Blvd., St. Louis.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: Memphis, Tenn., January. Sec., Dr. Fremont A. Chandler, 6 N. Michigan Ave., Chicago.

AMERICAN BOARD OF PEDIATRICS: Detroit, October 26; Rochester, N. Y., November 13; and Oklahoma City, November 15. Sec., Dr. C. A. Aldrich, 723 Elm St., Winnetka, Ill.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: New York, Dec. 28-30. Sec., Dr. Walter Freeman, 1028 Connecticut Ave. N.W., Washington, D. C.

AMERICAN BOARD OF RADIOLOGY: St. Louis, May 11-14. Sec., Dr. Byrl R. Kirklin, 102-110 Second Ave. S.W., Rochester, Minn.

AMERICAN BOARD OF UROLOGY: New York, Jan. 13-15. Sec., Dr. Gilbert J. Thomas, 1009 Nicollet Ave., Minneapolis.

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: Part III. Baltimore, Oct. 25-27, and Boston, Nov. 1-3. Med. Sec., Dr. J. Stewart Rodman, 225 S. 15th Street, Philadelphia.

Wisconsin June-July Report

Dr. Henry J. Gramling, secretary, Wisconsin State Board of Medical Examiners, reports the written and practical examination held at Milwaukee, June 28-July 1, 1938. The examination covered twenty subjects and included 100 questions. An average of 75 per cent was required to pass. Ninety-nine candidates were examined, all of whom passed. Twenty-eight physicians were licensed by reciprocity. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
University of Arkansas School of Medicine.....	(1937)	84	
College of (1938)	82		
University of (1934)	88*		
University of Georgia School of Medicine.....	(1937)	85	
Loyola University School of Medicine.....	(1938)	85	
Northwestern University Medical School.....	(1938)	81	
84, 86, 86, 88, 89			
Rush Medical College.....	(1937)	84, 85	
School of Medicine of the Division of Biological Sciences (1937)		86	
University of Illinois College of Medicine.....	(1938)	86, 87	
University of Louisville School of Medicine.....	(1937)	80, 84	
Tulane University of Louisiana School of Medicine.....	(1937)	85	
Harvard University Medical School.....	(1935)	88,	
(1937) 83, 84, 85, 86			
University of Minnesota Medical School.....	(1938)	84	
University of Nebraska College of Medicine.....	(1937)	80	
University of Rochester School of Medicine.....	(1937)	82	
University of Cincinnati College of Medicine.....	(1938)	84	
University of Oregon Medical School.....	(1936)	86	
University of Pennsylvania School of Medicine.....	(1937)	84, 85	
Marquette University School of Medicine.....	(1938)	80,	
80, 80, 80, 81, 81, 82, 82, 82, 83, 83, 83, 83, 83,			
84, 84, 84, 84, 84, 84, 85, 85, 86, 86, 86, 86, 86,			
87, 87, 88, 88, 89			
University of Wisconsin Medical School.....	(1935)	83,	
(1936) 83, 85, 86, 88, (1937) 81, 81, 83, 83, 84, 84,			
84, 84, 84, 84, 85, 85, 85, 85, 85, 85, 85, 86, 86,			
86, 86, 87			

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
George Washington University School of Medicine.....	(1933)		Ohio
Dearborn Medical College, Chicago.....	(1904)		Illinois
Loyola University School of Medicine.....	(1937)		Illinois
Northwestern University Medical School.....	(1910), (1937)		Illinois
Rush Medical College.....	(1922), (1936)		Illinois
School of Medicine of the Division of Biological Sciences.....	(1933) Illinois, (1936)		Kansas
University of Illinois College of Medicine (1934), (1936, 2), (1937, 2) Illinois			
Tulane University of Louisiana School of Medicine.....	(1932)		Louisiana
Johns Hopkins University School of Medicine.....	(1931)		Penna.
Univ. of Minnesota Medical School (1927), (1928), (1935)			Minnesota
St. Louis University School of Medicine.....	(1936)		Missouri
Washington University School of Medicine.....	(1934), (1936, 2)		Missouri
University of Nebraska College of Medicine.....	(1929), (1935)		Nebraska
University of Oklahoma School of Medicine.....	(1932)		Oklahoma
University of Pennsylvania School of Medicine.....	(1937)		Ohio
Marquette University School of Medicine.....			Ohio

* License withheld pending completion of internship.

Utah June Report

Mr. S. W. Golding, director, Department of Registration, reports the written examination held by the State Board of Medical Examiners at Salt Lake City, June 27-29, 1938. The examination covered ten subjects and included 100 questions. An average of 75 per cent was required to pass. Twelve candidates were examined, all of whom passed. Six physicians were licensed by reciprocity and one physician was licensed by endorsement. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
University of Colorado School of Medicine.....	(1938)	83*	
George Washington University School of Medicine.....	(1937)	83, 85	
Northwestern University Medical School.....	(1938)	84, 85	
Rush Medical College.....	(1937)	80, 82, 84*	
University of Louisville School of Medicine.....	(1937)	83	
Harvard University Medical School.....	(1935)	86	
Washington University School of Medicine.....	(1938)	81*	

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
University of Colorado School of Medicine.....	(1937)		Colorado
Northwestern University Medical School.....	(1937)		Illinois
State University of Iowa College of Medicine.....			Iowa
Washington University School of Medicine.....			Missouri
University of Nebraska College of Medicine.....	(1934)		Nebraska

School	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
George Washington University School of Medicine.....	(1936) N. B. M. Ex.		

* License withheld pending completion of internship.

Virginia June Report

Dr. J. W. Preston, secretary, Board of Medical Examiners of Virginia, reports the written examination held at Richmond, June 22-24, 1938. The examination covered eight subjects and included eighty questions. An average of 75 per cent was required to pass. One hundred and fifteen candidates were examined, all of whom passed. Twenty-seven physicians were licensed by reciprocity and nine physicians were licensed by endorsement. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
University of Arkansas School of Medicine.....	(1936)	86	
Georgetown University School of Medicine.....	(1937)	83,	
Howard University College of Medicine.....	(1937)	78, 79	
Rush Medical College.....	(1938)	82	
Temple University School of Medicine.....	(1938)	84	
Woman's Medical College of Pennsylvania.....	(1937)	82	
Medical College of Virginia.....	(1936)	82,	
(1938) 78, 78, 79, 79, 79, 79, 80, 80, 80, 80, 81,			
81, 81, 81, 81, 81, 82, 82, 82, 84, 84, 84, 84, 84,			
84, 84, 84, 84, 85, 85, 85, 85, 85, 85, 85, 85, 86, 86,			
86, 86, 86, 86, 87, 87, 87, 88, 88, 88, 89, 90			
University of Virginia Department of Medicine.....	(1938)	77,	
79, 79, 79, 80, 82, 82, 82, 83, 83, 83, 83, 83,			
83, 83, 84, 84, 84, 85, 85, 85, 85, 85, 85, 85, 85,			
85, 86, 86, 86, 86, 86, 86, 86, 86, 86, 87, 87, 87,			
87, 87, 87, 88, 88, 89, 89, 90			
University of Wisconsin Medical School.....	(1935)	79	
University of Manitoba Faculty of Medicine.....	(1932)	84	
Schlesische-Friedrich-Wilhelms-Universität Medizinische Fakultät, Breslau.....	(1935)	81	
Regia Università degli Studi di Palermo. Facoltà di Medicina e Chirurgia.....	(1931)	78	

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
Stanford University School of Medicine.....	(1937)		California
University of Colorado School of Medicine.....	(1931)		Colorado
Emory University School of Medicine.....			Georgia
Loyola University School of Medicine.....			Illinois
University of Louisville School of Medicine.....			Kentucky
Louisiana State University Medical Center.....	(1934)		Louisiana
Johns Hopkins University School of Medicine.....	(1935)		Maryland
University of Maryland School of Medicine.....	(1901)		Maryland
University of Maryland School of Medicine and College of Physicians and Surgeons.....	(1934), (1936)		Maryland
New York Homeopathic Medical College and Flower Hospital.....	(1915)		New York
University of Cincinnati College of Medicine.....	(1935)		W. Virginia
Temple University School of Medicine.....	(1933)		Penna.
Univ. of Pennsylvania School of Medicine.....	(1934) Dist. Colum.,		Penna.
University of Pittsburgh School of Medicine.....	(1925)		Penna.
Medical College of the State of South Carolina.....	(1937)		S. Carolina
Melarry Medical College.....	(1937)		Tennessee
University of Tennessee College of Medicine.....	(1934), (1936)		Tennessee
Vanderbilt University School of Medicine.....	(1913)		Kentucky
(1932), (1936) Tennessee			
Baylor University College of Medicine.....	(1933), (1934)		Texas
University of Virginia Department of Medicine.....	(1925) Dist. Colum,		

School	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
Yale University School of Medicine.....	(1934) N. B. M. Ex.		
George Washington University School of Medicine.....	(1936) N. B. M. Ex.		
Johns Hopkins University School of Medicine.....	(1922), (1933) N. B. M. Ex.		
Detroit College of Medicine and Surgery.....	(1922)		U. S. Navy
University of Michigan Medical School.....	(1934) N. B. M. Ex.		
Duke University School of Medicine.....	(1934), (1935) N. B. M. Ex.		
University of Oklahoma School of Medicine.....	(1927) N. B. M. Ex.		

Book Notices

A Textbook of Gynecology. By Arthur Hale Curtis, M.D., Professor and Chairman of the Department of Obstetrics and Gynecology, Northwestern University Medical School, Chicago. Third edition. Cloth. Price, \$7. Pp. 603, with 318 illustrations chiefly by Tom Jones. Philadelphia & London: W. B. Saunders Company, 1938.

Here is a volume which may well serve as a model for gynecologic textbooks of the future. From the beginning the reader realizes that the author is drawing on his mature experience and an intimate knowledge of the literature, and not on hearsay and hand-me-downs. He has succeeded in covering the essentials of gynecologic knowledge concisely and adequately. His long experience as a clinician has enabled him to compile his book with a fine sense of proportion; for example, thirty-eight pages are given to gonorrhea, three pages to endometritis. Only the section on urology in gynecology seems unduly condensed. The writing is excellent, always clear, often elegant. It is easy and pleasant reading. The best American opinion has been summarized with almost no personal bias. Yet Dr. Curtis has retained his own voice and in many places has gracefully disagreed with the consensus. In each such instance he has taken pains that his dissenting opinion shall be regarded as an individual, and not as a generally accepted belief. The tone of the volume is forcefully conservative. One feels that only after long disappointment with conservative methods has the author been willing to accede to any radical procedure. An exception to this conservatism is his intimation that surgery may be preferable to radium in the treatment of very early carcinoma of the cervix. The reviewer takes no issue with Dr. Curtis's beliefs but does feel strongly that his textbook is not the proper place to express an opinion which may lead to a dangerous reversal in gynecologic practice. So uniform is the high quality of the work that it is difficult to cite the "best" features. Possibly the first section of the book is most satisfying. Here the anatomy of the female pelvis is presented as every gynecologist wishes to see it: academic anatomy, physiology, pathology, pathologic anatomy and surgical aspects equally emphasized. Dissections undertaken especially for this textbook have clarified several poorly understood relations. The illustrations by Cassell, McHugh and Jones and the photographs are excellent; the photomicrographs are fair. The references, which are generous, include the full title of the quoted articles, a practice to be highly commended. This textbook is suitable for undergraduates but will be of particular value to interns. It should be read by every physician who treats gynecologic diseases. When he finishes the volume the reader will wonder whether 600 pages could possibly contain a finer exposition of fact, experience and good judgment in gynecology.

La fibrose pulmonaire des mineurs. Par Louis Croizier, médecin des hôpitaux de Saint-Etienne, Edme Martin, médecin-chef des dispensaires départementaux d'hygiène sociale de La Loire, et Albert Polleard, professeur à la Faculté de médecine de Lyon. Paper. Price, 165 francs. Pp. 214, with 186 illustrations. Paris: Masson & Co, 1938.

The book is based on clinical, roentgenographic and post-mortem examination of a group of coal miners. Without giving data on the nature of the coal or dust concentrations, the authors have accepted employment records of work in rock or coal and attempted to differentiate the pulmonary reactions resulting from inhaling the two kinds of dust. They fail to point out, however, that the anthracosilicosis with which they have dealt may be different from that in other industries in which coal dust is not present. They have not been able to classify the roentgenologic appearances according to any of the generally accepted schemes but describe them in the following groups: ill defined diffuse shadows; nodular shadows; unilateral or bilateral dense shadows; pseudo-tumor-like shadows. The picture of linear exaggeration, called in South Africa "more fibrosis than usual," they were not able to identify.

They failed to find the roentgenogram as valuable an aid in diagnosis as most other observers have done. In fact they conclude that, while it is of value in establishing the existence of a pulmonary lesion, it cannot determine the nature of the

lesions. They argue that, since individual tubercles and silicotic nodules have similar morphology, they must cast identical shadows. No reference is made to the difference in distribution and the resultant disease patterns on which most roentgenologists rely so strongly nor do they mention differences in the evolution of the pathology of silicosis and tuberculosis. They do admit that serial roentgenograms are more helpful than single films but even these they use merely as a check on the clinical and bacteriologic evidences of disease.

The fact that many of the miners who were reported to have worked in rock for years showed no evidence of disease convinced them that variations in individual susceptibility must have been present in others who did acquire silicosis. The high frequency of obvious tuberculosis among the group as a whole convinced them that this was the variable factor responsible for the susceptibility of the miners who exhibited silicotic nodulation. They therefore adopted the idea held by older observers that silicotic nodulation is always associated with an element of infection. A novel explanation is proposed for the evolution of the disease as either discrete nodulation or as manifest tuberculosis complicating silicosis. In the first instance the authors suggest infection with attenuated tubercle bacilli, in the second with organisms of full virulence. They even propose to institute hygienic dietetic treatment of the cases with generalized nodulation in the hope that the infectious element will heal and the nodules disappear.

The well recognized frequency of so-called conglomerate fibrosis in coal miners has made their problem difficult, but they do not adopt the concept of "silicotuberculosis" as ordinarily accepted. Atelectasis from bronchial occlusion in their minds is responsible for many of the massive areas of fibrosis.

Immune-Blood Therapy of Tuberculosis with Special References to Latent and Masked Tuberculosis. By Joseph Hollés, M.D. Cloth. Price, \$2. Pp. 197. New York: The Author, 1938.

The author has had a stormy course. In an introduction of approximately ten pages he describes how his point of view was developed and how he began to experiment with immune blood in 1908. However, when he presented his work to the medical world it was severely attacked. Only rarely did he find a physician who gave it any consideration. He first published a book entitled "Tuberculous Intoxications," from Budapest. In 1911 his book was awarded a prize of a thousand francs by the Academy of Medicine in Paris. He claims that about the time his ideas were to be accepted in Germany Dr. Graefenberg reaped the benefit, when a German medical congress in Wiesbaden handed him the laurels.

After the World War he was about to undertake the task of freeing Budapest of tuberculosis in a twenty year period, but the failure of the political party with which he was allied put an end to this undertaking. A little later the Tuberculosis Association of Hungarian Physicians expelled him from membership. In order "to escape imprisonment or murder" he emigrated, finally reaching the United States. New York was the eighth place in which he settled after leaving Budapest. In America he found that the treatment of tuberculosis was decades behind that of Europe. Despite the fact that he believed he could free any metropolis of tuberculosis by his immune-blood therapy in a short time, he was unable to obtain a position in any hospital or sanatorium as a tuberculosis specialist. Even his manuscripts were rejected by the American medical journals. He could not find a place on first class medical programs. He had a question sent to *THE JOURNAL* concerning immune blood but it was returned with a statement to the effect that investigation had shown such therapy in tuberculosis to be ineffective. When his work was not accepted in American medical journals he found a publisher in Edinburgh, Scotland, who published a book for him under the title of "Tuberculous Intoxications: Concealed and Masked Tuberculosis." This appeared in 1928, after seven American publishers had returned his manuscript. He sent copies to well known physicians and numerous medical institutions and especially called it to the attention of the Health Commissioner of the city of New York. In his introduction he states that he was told that the National Tuberculosis Association does not like new ideas and, therefore, "put thumbs down on the book."

and prevented its circulation." Two years later he learned that only seventy copies of his book had been sold in the entire United States. Ten years have now passed since the appearance of his last book and the author feels it necessary "to communicate again with the medical world."

The subject matter of this volume is of such a nature that the book will probably be received with as little enthusiasm as the previous book, if not less. So little has actually been proved about immunity in tuberculosis that it is impossible to understand the rationale of such treatment. The author's immune blood is obtained from "immunized" rabbits. His preparation is administered in two ways: He gives a subcutaneous injection every two or three weeks and during the interim the patient rubs some of the material into the skin once every day or so. In connection with this, which he calls specific treatment, he believes that rest, hygienic and dietetic treatment are also advisable. However, he claims excellent results in many cases without the patient discontinuing his work. The author cites seventy-eight cases, in a good many of which the evidence of tuberculosis is so flimsy as to leave considerable doubt in the mind of the reader as to whether this disease actually existed in clinical form. He cites the cases of some children who from the evidence presented would appear to have had nothing more than primary tuberculosis complexes. A series of patients suffering from neurasthenia, rheumatism, thyrosis, dementia praecox, epilepsy, dysmenorrhea, disturbances of the digestive system and other symptom complexes was treated with immune blood on the ground that these conditions were due to tuberculous lesions somewhere in the body and the later abatement of symptoms is presented as proof of the specificity of this treatment. Every clinician who has had an extensive experience in tuberculosis therapy can select from his files as many or more cases that responded in a similar manner as those here cited in the absence of immune blood administration. Many tuberculous lesions enter on long periods of remissions without any treatment whatever. The nature of tuberculosis is such that the citation of only seventy-eight cases with such a large variety of symptoms and so little evidence of the disease having existed in clinical form in many of them proves nothing.

Typhoid Fever on the Witwatersrand: Bacteriological Aspects, Serological Diagnosis, Specific Prophylaxis and Specific Treatment. By W. Lewin, M.D., B.Ch., D.P.H. Thesis Accepted for the Degree of Doctor of Medicine in the University of the Witwatersrand, Johannesburg. Publications of the South African Institute for Medical Research. No. XLII, Vol. VII. Edited by the Director. Paper. Pp. 413-550, with 25 illustrations. Johannesburg: The Institute, 1938.

The observations recorded in this monograph are considered under four headings noted in the title. The work which forms the basis of the report was carried out among native mine workers in an area where typhoid is widely prevalent. As the author states, the workers lived under "herd" conditions. Food was served to several thousand from one kitchen. The sewage disposal was crude, the bucket system being used underground. The miners were largely non-Europeans, who worked in the mines an average of nine months, thereafter returning to their native "kraal." Some 300,000 men were thus employed, among whom the carrier rate was 2 per cent.

The section on bacteriologic aspects deals largely with strains isolated from blood and excreta, classified according to the method of Kaufman. The majority of strains were found to belong in Kaufman's V-W group, containing Vi antigen. The V type with a preponderance of Vi antigen was found infrequently (eighteen of 299 strains), while the W type with Vi antigen absent (four of 299 strains), was recovered still less frequently. The work of Felix and others concerning the agency of Vi antigen in determining mouse virulence and immunizing potency is confirmed; the author finds as do others that there is the discrepancy between the observed severity of the disease and the virulence of the infecting organism; that is, there is no correlation between the high pathogenicity that strains rich in Vi antigen exert on mice and the moderate course of the infection in human beings from whom strains rich in Vi antigen have been isolated.

The section on serologic diagnosis is largely given over to a consideration of O and H agglutination titers. An attempt

is made to determine a diagnostic level, and this the author fixes at 1:100 for the H antigen and 1:200 for the O antigen. These titers he adopted because (a) a false positive was likely to be ruled out and (b) a clinical attack of typhoid generally results in titers higher than those adopted. He tested his diagnostic titers by agglutination tests in two series of cases admitted to the hospital with the diagnosis of enteric fever. There was a high correlation noted between the cases in which *Bacillus typhosus* was isolated from blood or excreta and the author's diagnostic agglutination titers.

In the section on prophylaxis the "typhoid endotoxoid" of Grasset (prepared by formalization of frozen and thawed bacterial suspensions) is compared with oral typhoid tablets prepared from the same strains and with TAB vaccine. The results with oral administration of typhoid vaccine were poor and confirms the work of others. The author concludes from his observations and the work of others on the inoculation of mine personnel that the vaccine of choice is "typhoid endotoxoid" for the reason that it is efficacious and because there is a minimum of general reactions following its use.

Serum therapy was used in sixty-two cases, and these are compared with 625 controls. Because of the small number of cases treated, age and sex were not considered. Although the case mortality was somewhat lower among the serum treated, the conclusion that it is significantly different in the two groups is hardly warranted, particularly with such a disproportion between serum treated and controls, the while ignoring age and sex. A small series of cases were treated with serum in which Vi antibodies were included. Brief case reports and fever charts are appended. Results appear encouraging. Finally, a small number of cases treated with increasing doses of "typhoid endotoxoid" vaccine is recorded, apparently resulting in a reduction in the mortality rate. The use of serum followed by inoculation with "typhoid endotoxoid" is mentioned as a possible means of treatment of known cases.

Much effort has been expended in the preparation of this monograph. For some studies too few observations are recorded, and one wonders whether a consideration of fewer aspects of the problem might not have resulted in more conclusive studies rather than in a work which apparently confirmed that of others but which by itself appears only indicative. This criticism appears more pertinent in the light of the unexcelled opportunity for study afforded by the incidence of typhoid among so large a group of mine workers.

In many instances, references to the work of others applied to the particular phase of the work discussed is given, and section bibliographies are ample. This is desirable, but when in the instance of agglutination studies the "... investigation was carried out primarily to confirm the results obtained by Felix and his co-workers on the antigenic properties of *B. typhosus* in regard to the Vi antigen ..." one wonders what effect wishful planning has had on some of the work here reported. Finally, the investigative opportunity afforded by a high prevalence of typhoid creates a difficulty with respect to certain phases of the study, particularly serologic diagnosis. Where it is impossible to determine accurately whether persons have a negative history of typhoid or of previous inoculation against the disease, the question of subclinical infection cannot be ruled out, thus affecting controls utilized in certain comparisons.

This monograph should be read by all whose clinical, laboratory or administrative duties involve contact with one or more phases of the typhoid problem.

A Textbook of Clinical Pathology. Edited by Roy R. Kracke, Emory University, Ga. Cloth. Price, \$6. Pp. 567, with 236 illustrations. Baltimore: William Wood & Company, 1938.

The late Foster M. Johns of Tulane University had organized and nearly finished the work of this book at the time of his death in 1936. It represents the cooperative efforts of twelve different contributors, brought to completion under the editorship of Roy R. Kracke of Emory University. The use of multiple authors in the writing of a textbook of clinical pathology is commendable. There is probably no clinical pathologist today who is so thoroughly grounded in physiologic chemistry and serology and hematology, for instance, that he could be considered a first rank authority in all these fundamental branches of clinical pathology. Yet those who

expect to find in this book something altogether new or extraordinary will be disappointed. The book has distinct merit but, taken as a whole, it is not exceptional.

The introduction to each subject clearly states the problems to be considered and their importance. Following descriptions of methods and technic there is usually a discussion on the interpretation of the results. These explanatory paragraphs are usually clear, concise and inclusive. The chapters on hematology are especially good. In thoroughness and lucidity they are probably not excelled in works similar to this. They occupy nearly half of the book. The chapters dealing with bacteriologic methods also are excellent. They are unusually complete, and the methods given are exceptionally well chosen. Unfortunately, this material is rather scattered. The chapters on sputum and urinalysis are unduly brief. Indeed, they are nearly inadequate. This is perhaps the result of efforts to confine the book to its present convenient size. Some of the newer tests, such as those for alcohol, bromide and heterophile antibody are included; but other simple and relatively important tests, such as those for sulfanilamide and amyloidosis are omitted. Serologists may protest the inclusion of the syphilis tests of Johns and Laughlin in preference to the more generally recognized tests of Hinton and Eagle. An excellent feature is the inclusion of a list of original references at the end of each of the principal sections of the book.

This book is not an important addition to the already rather well loaded laboratory bookshelf but it is a good book and will no doubt become popular with the students, clinicians and small hospital laboratories for which it was written.

Handbuch der experimentellen Pharmakologie. Begründet von A. Heffter. Ergänzungswerk. Herausgegeben von W. Heubner, Professor der Pharmakologie an der Universität Berlin, und J. Schüller, Professor der Pharmakologie an der Universität Köln. Band VI: Enthaltend Beiträge von O. Gessner und G. Barger. Paper. Price, 30 marks. Pp. 245, with 54 illustrations. Berlin: Julius Springer, 1933.

In previous reviews of these supplements to Heffter's *Handbuch*, we have emphasized the importance of the work to research workers and to others who wish a complete survey of the drugs discussed. The present supplement contains but two subjects: (1) *Tierische Gifte* (Poisons of Animal Origin), by Professor Gessner of Halle, and (2) *The Alkaloids of Ergot*, by Professor Barger of Glasgow. The original article on *Tierische Gifte* was written by Professor Edwin Santon Faust in volume I², page 1748, published in 1924, and occupies 265 pages. The present supplement deals mainly with the developments since 1924 and occupies eighty-three pages. The references to the literature are extensive. The practicing physician will find this an interesting subject and will perhaps be amazed at the wide occurrence of poisonous substances in animals. He will find the known pharmacologic actions, and considerable chemistry that may aid him in practice, but no direct therapeutic uses or treatment. The original article on ergot in this handbuch (volume II², pp. 1297-1354) was written by the late Prof. Arthur Cushny in 1914 but was not published until 1924, without further revision. Thus a gap of two decades is now filled by Professor Barger. The present work is almost as large as the original, and since the best work on ergot has been done since the Cushny article was written, it is much more important. The original article was in German, the present is in English. Those acquainted with Professor Barger or his work know what to expect.

Essentials of Obstetrical and Gynecological Pathology with Clinical Correlation. By Marion Douglass, M.D., F.A.C.S., Assistant Professor of Gynecology, Western Reserve University, Cleveland, Ohio, and Robert L. Faulkner, M.D., Senior Clinical Instructor in Gynecology, Western Reserve University. Cloth. Price, \$4.75. Pp. 187, with 148 illustrations. St. Louis: C. V. Mosby Company, 1933.

This small monograph on the essentials of obstetric and gynecologic pathology was meant to fill a long standing need in modern American textbooks. To date there has been no volume limited to the pathology of obstetrics and gynecology, and many teachers have felt the necessity for just such a work. This book is well illustrated and simply written—in fact, one has the definite feeling that the authors have made the text too simple. True, they have set out to write a book for "the student beginning his acquaintance with the special pathology

of this field and to the clinician who may want to review the essential histopathology of his specialty," but to a teacher of this subject to both students and interns the book seems inadequate. The text is meager and incomplete, there is no bibliography, and many topics have been omitted completely.

Historia del protomedicato de Buenos Aires. Estado de los conocimientos sobre medicina en el Rio de la Plata, durante la época colonial. Los galenos españoles y los magos o curanderos indígenas. Antecedentes históricos y legales de la fundación del protomedicato y de la Escuela médica de Buenos Aires. Por Juan Ramon Beltrán, profesor adjunto de medicina legal en la Facultad de ciencias médicas. Paper. Pp. 316. Buenos Aires: El Ateneo, 1937.

The history of the protomedical center of Buenos Aires is of interest in relation to the development of medicine in Argentina. Dr. Beltrán's book on the subject is an exposé of printed or photographic authentic copies of historical documents which show the actual conditions of medicine in Argentina during the Spanish colonial period and its development up to the establishment of the University of Buenos Aires. Originally the protomedical center was the board of Spanish physicians who were in charge of the health and sanitary problems of the Spanish colonies, including teaching, examination and license of candidates to practice in the colonies. These problems in Argentina were under the control of the board of Lima. The protomedical board and center of Buenos Aires was established in 1778 by the viceroy Vertiz at the request of the Spanish physicians Miguel Gorman and Augustin Eusebio Fabre. It developed later on with the collaboration of Cosme Argerich, an Argentine-Spanish physician, into a small organized center for medical education with clinical and surgical departments and also a center for medical military services. The first school of medicine of Buenos Aires opened in 1800. It was under the supervision of the protomedical center. The latter disappeared in 1822 when the University of Buenos Aires was organized. Dr. Beltrán's book is interesting as it shows the development of medicine with the evolution of Argentina as an independent nation and also the example and self denial of physicians who fought for the advance of medicine for posterity.

The Chemistry of the Steroids. By Harry Sobotta, Chemist to the Mount Sinai Hospital, New York. Cloth. Price, \$8.50. Pp. 634. Baltimore: Williams & Wilkins Company, 1933.

Chemical investigation has stimulated new formulations for the bile acids, sterols, the cardiac glycosides, sex hormones, and the antirachitic vitamins which have been recognized as phenanthrene derivatives, thereby increasing their numbers many fold in a short time. The author has developed an extensive list of the steroids, giving their physical and physiologic properties and discussing various analytic methods used in physiologic experimentation on the bile and sterols. The clinician will find valuable data in this comprehensive compilation of the bile acids and their related compounds. It is an excellent textbook for a reference library.

A. M. A. Interns' Manual. Edited by the Council on Medical Education and Hospitals and the Council on Pharmacy and Chemistry of the American Medical Association. Fabrikoid. Price, 60 cents. Pp. 222. Chicago: American Medical Association, 1933.

Every change made in this volume has been an improvement. Its size—an important feature to the overloaded intern—has been reduced, yet the information it offers has been materially increased. Besides an epitome of useful drugs and other forms of therapy usually administered by the intern, it also contains data on diets, toxicology and numerous practical hints. An important feature is that section concerning the intern's duties to the hospital and its personnel and what he in turn should expect from them. This vital part has been greatly neglected in the past. The hospital administration, the medical staff and the intern must realize that the so-called stipend, while desirable, can in no way compensate for certain elemental training at present denied to many interns. The intern is always a student, never a paid servant. Some of the faults of certain practitioners today certainly are traceable to defective internships. Hospital staffs and local medical societies might provide each intern with one of these valuable manuals and take a more active part in the welfare and guidance of the intern with wholly beneficial results to the medical profession.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Middle Ear Infection and Mastoiditis in Relation to Trauma.—On Jan. 4, 1934, when a school bus operated by the defendant turned over, the plaintiff's son collided with or was thrown against a boy sitting opposite him in the bus. Within thirty minutes thereafter he complained of pain in the region back of his left ear. That evening he complained to his mother of a pain in the back of his neck and around his left ear. His mother applied "home remedies," using a liniment and hot towels, and continued to do so for the next two weeks. On January 20 a physician sent the boy to a hospital and on January 23 diagnosed the case as one of "a middle ear infection with a mastoid involvement." Notwithstanding a surgical operation, the boy died on February 14. The plaintiff, as administrator of the estate of his deceased son, brought this action against the driver of the bus. From a verdict in favor of the plaintiff, the defendant appealed to the Supreme Court of Iowa, alleging among other things that the trial court erred in overruling a motion for a directed verdict in the defendant's favor, because the plaintiff had not submitted evidence justifying the submission of the case to the jury.

At the trial, two expert medical witnesses for the plaintiff, in answer to hypothetical questions, testified that "an infection in the inner ear could or might result from trauma or a blow" and that "a bruise, without even a puncture or a rupture of the membrane itself, but just the bruise of the inner ear, that in itself could in time become sufficiently aggravated to go through this period of incubation and create an infection in the inner ear." The physician who attended the boy and who presumably performed the operation testified that in his judgment an injury was the probable cause of the mastoiditis which caused the boy's death. There was medical testimony that scarlet fever, which the boy had had some eight to ten years prior to the accident and from which he had recovered, could not have been the cause of the mastoiditis. Medical testimony for the defendant, however, was to the effect that trauma was not the cause of the boy's death.

The Supreme Court was of the opinion that the evidence presented was sufficient to warrant the trial court in submitting the case to the jury. The evidence showed that the plaintiff's son was physically fit prior to the accident but within thirty minutes thereafter he complained of a pain back of his left ear, that in the evening he complained to his mother of pain in the same region, and that from that time until his death he was treated by his mother or by physicians. In the opinion of the court the medical testimony eliminated all probable causes of mastoiditis other than trauma. Accordingly, the Supreme Court affirmed the judgment of the trial court in favor of the plaintiff. —*Olson v. Cushman (Iowa)*, 276 N. W. 777.

Workmen's Compensation Acts: Compensability of Death Due to Sepsis.—Easton, in the course of his employment in the "scrub house" of the defendant's tannery, handled wet leather. His hands constantly came into contact with a tanning fluid that caused "cracks" on the fingers and hands of the workmen. After complaining while still at work of a "crack" on his left index finger for some weeks, he had to quit work, and after a few days treatment at home he was taken to a hospital. On admission, he had a high temperature and "a swollen condition of the left shoulder and axilla and a lump over his heart." Several weeks later he died. His widow brought proceedings under the workmen's compensation act of Pennsylvania against his employer. The workmen's compensation board awarded compensation on the ground that Easton had died "from a streptococcal infection of the blood stream . . . due to a septic poisoning which he contracted . . . through the sore or crack which he had on the index finger of his left hand, which he received in the handling of the wet hides." The employer apparently appealed to the court of

common pleas; Potter County, and from a judgment of that court reversing the board's award the claimant appealed to the superior court of Pennsylvania.

The physician who attended Easton at the hospital testified in the course of the proceedings that when first examined he had a "crack" in his left index finger and blisters in the palm of his hand; that he had contracted an infection which entered the lymphatics of the palmar surface of the hand and traveled upward to the lymphatic glands of the armpit, where it "centralized," and that later the infection had entered his blood stream, as was demonstrated by examinations of the blood. In his opinion the absence of swelling of the hand and forearm was not significant, because evidence of infection is not always present at the site of entrance of the infecting bacteria. Another physician, who had attended the deceased prior to his admission to the hospital, testified that it is not always possible to determine the portal of entrance of the bacteria that later infect the blood stream. The superior court concluded that the evidence adduced did not support the board's finding that the infection had entered the blood stream of the deceased "through the sore or crack which he had on the index finger of his left hand."

Even assuming that there was testimony to support an inference that the infecting germ entered Easton's body through a "crack" on his finger, the entry of the germ, in the judgment of the court, was not brought about by an accidental injury occurring in the course of his employment. The evidence showed that the germ may have entered his body when he was absent from the premises of his employer and while engaged in activities having no connection with his employer's business. An "injury" or "personal injury" is defined by the workmen's compensation act to mean "only violence to the physical structure of the body, and such disease or infection as naturally results therefrom." In the instant case there was no abrupt or unforeseen external or internal "violence to the physical structure" of the deceased's body. There was no untoward or unexpected occurrence. The "sore or crack" on Easton's hand was a natural and usual incident of the kind of work in which he was engaged. This was a case of death from a germ disease which, whether it developed from germs within the body or from germs from without, was not due to an accidental injury and was not compensable.

Accordingly the superior court affirmed the judgment of the lower court reversing the workmen's compensation board's award of compensation.—*Easton v. Elk Tanning Co. (Pa.)*, 195 A. 648.

Workmen's Compensation Acts: Compensability of Paralysis Due to Cerebral Thrombosis.—Custer, a master mechanic employed by the London Gold Mines Company, continued to work at an altitude of over 10,000 feet although he had been advised by a physician three months before that he should work at a lower altitude because he had a "secondary polycythemia." One evening, after walking up a steep grade for a distance of 350 feet in order to get to his office, he collapsed and became unconscious. Later he became totally disabled by paralysis of his right side, due to a thrombosis or a ruptured blood vessel in his brain. He brought proceedings under the workmen's compensation act against his employer and its insurance carrier, claiming that his paralysis was due to a ruptured blood vessel caused by his climb and the resulting exhaustion. The industrial commission, however, denied compensation on the ground that the claimant's paralysis was due to a cerebral thrombosis resulting from "secondary polycythemia" and not the result of an accident or external injury. From a judgment of a district court, to which an appeal had been taken, reversing the award of the industrial commission, the employer, the insurance carrier and the commission appealed to the Supreme Court of Colorado.

The medical testimony presented before the commission was to the effect that the claimant's paralysis was not due to his employment and would have occurred regardless of what he was doing at the time. One medical witness testified that, regardless of whether a rupture or a thrombosis of a cerebral blood vessel had occurred, there was no connection between

such an occurrence and an industrial accident. Two medical witnesses were of the opinion that the paralysis was due to a cerebral thrombosis. One of these witnesses, who was of the opinion that thrombosis of the left internal carotid artery had occurred as the result of physical illness and not the result of an accident, in answer to a question as to whether exertion might have accelerated the attack, testified: "If it is a hemorrhage of the brain I think it is possible, yes; if thrombosis I would say, no."

While there was some evidence, said the Supreme Court, from which the commission might have found that the paralysis was due to a rupture of a cerebral blood vessel primarily caused by overexertion, such a finding would have been contrary to the preponderance of the evidence. The court concluded, therefore, that the commission's finding that the paralysis was due to a cerebral thrombosis, with no industrial connection, was amply supported by the evidence. Accordingly, the Supreme Court reversed the judgment and remanded the cause to the lower court with directions that the commission's order disallowing compensation be affirmed.—*Louden Gold Mines Co. et al. v. Custer (Colo.)*, 74 P. (2d) 679.

Medical Practice Acts: Chiropractor May Neither Practice Physical Therapy Nor Prescribe Diets.—The defendant, a licensed chiropractor in Iowa, held himself out, including the using of newspaper and telephone directory advertising, as practicing physiotherapy, electrotherapy, and colonic irrigation, and as prescribing diets. In some advertisements he designated himself as being a chiropractor and physiotherapist. Contending that these practices constituted the practice of medicine, not the practice of chiropractic, the state instituted proceedings to enjoin the defendant from continuing such methods of treatment. The district court issued the injunction but provided that the decree should not enjoin the defendant "from using his reasonable judgment in recommending to a patient certain changes of diet, exercise or such of his general habits as affect his health." From this portion of the decree the state appealed to the Supreme Court of Iowa, claiming with respect thereto that the prescribing of diets should have been wholly enjoined. The defendant chiropractor appealed from the decree as a whole.

The practice of chiropractic in Iowa is defined by statute as "the adjustment by hand of the articulations of the spine or by other incidental adjustments." In this act, said the court, is found the only source of the defendant's authority to treat human ailments. When he professed to use and used modalities other than those authorized, as curative means or methods, he attempted to function outside of the restricted field of endeavor to which the legislature limited his practice. The defendant contended that another section of the chiropractic act, section 2559, authorized, by inference, the type of practice in which he was engaged by providing that a license to practice chiropractic shall not authorize the licensee to practice operative surgery or osteopathy, or to administer or prescribe any drug or medicines included in materia medica. Relying on the maxim "*expressio unius est exclusio alterius*," or the mention of one is the exclusion of another, he urged that because the thing prohibited in this section is the administering or prescribing any drug or medicine included in materia medica, a legislative intent was shown to authorize chiropractors to use medicine in the broad general definition of a remedial agent or remedy. He pointed to the fact that the section did not add the words "vibrator," "traction tables," "ultraviolet rays," "infra red lamps," "galvanic current," to the prohibitory words used therein and that it was obvious that the words could not be added except by the legislature. With this contention, the court expressed disagreement. The legislature intended, the court thought, to limit chiropractors in their treatment to the adjustment by hand of the articulations of the spine or by other incidental adjustments, and that section 2559 did nothing more than to emphasize the prohibition as to materia medica.

The Supreme Court approved the decree of the trial court restraining the defendant from professing to treat and treating human ailments in modes and manners outside the field of

chiropractic but held that the decree should have also enjoined him wholly from the prescribing for or the advising of his patients with respect to diet. The trial court was directed to revise the decree accordingly.—*State v. Boston (Iowa)*, 278 N. W. 292.

Workmen's Compensation Acts: Use of Corrective Lenses in Relation to Evaluation of Loss of Vision.—Elder, who had a total loss of vision in his left eye, injured his right eye in the course of his employment. He brought proceedings under the workmen's compensation act against his employer and its insurance carrier and was awarded compensation by the industrial commission for total industrial blindness. From a judgment by a district court, to which an appeal had been taken, sustaining that award, the employer and its insurance carrier appealed to the Supreme Court of Colorado.

The appellants claimed that the commission and the district court erred in failing to evaluate the claimant's vision with the correction obtainable by the use of lenses. The Supreme Court admitted that the authorities were in conflict as to whether corrective lenses should be used in the evaluation of loss of vision. In *Masoner v. Wilson & Co.*, 141 Kan. 882, 44 P. (2d) 265, it was held that the extent of loss of vision should be calculated irrespective of what it would scientifically be rated by applying corrective lenses. On the contrary, in *Kelley v. Prouty*, 54 Idaho 225, 30 P. (2d) 769, it was held that improvement by the use of corrective lenses must be considered in evaluating loss of vision. The Supreme Court, however, refused to undertake to reconcile these two views or to determine whether a sounder view lay somewhere between them. It decided only that the record in the case before it did not justify a rejection of the commission's finding that the claimant was industrially blind in his right eye and that he had a total loss of vision in his left eye prior to the accident. The court pointed out specifically that it did not say that there might not be a state of facts that would make correction with lenses an important factor in determining whether, under those facts, the reduction of loss of vision by the use of corrective lenses would be sufficient to remove the case from the class of total industrial loss. In the present case, however, the court concluded that it would not be in accord with the liberal nature of the workmen's compensation act to presume, in the absence of evidence so showing, that the use of corrective lenses would render the claimant partially efficient as an industrial worker, when without the use of such lenses he would be a total industrial loss.

Accordingly, the Supreme Court affirmed the judgment of the lower court affirming the commission's award.—*Philo Rogers, Inc. et al. v. Industrial Commission et al. (Colo.)*, 74 P. (2d) 673.

Society Proceedings.

COMING MEETINGS

- Academy of Physical Medicine, Washington, D. C., Oct. 24-26. Dr. Herman A. Osgood, 144 Commonwealth Ave., Boston, Secretary.
- American Public Health Association, Kansas City, Mo., Oct. 25-28. Dr. Reginald M. Atwater, 50 West 50th St., New York, Executive Secretary.
- American Society of Tropical Medicine, Oklahoma City, Nov. 15-18. Dr. E. Harold Hinman, Wilson Dam, Ala., Secretary.
- Association of American Medical Colleges, Syracuse, N. Y., Oct. 24-26. Dr. Fred C. Zapffe, 5 South Wabash Ave., Chicago, Secretary.
- Central Society for Clinical Research, Chicago, Nov. 4-5. Dr. Lawrence D. Thompson, 4932 Maryland Ave., St. Louis, Secretary.
- International Society of Medical Health Officers, Kansas City, Mo., October 24. Dr. Leon Banov, County Health Department, Charleston, S. C., Secretary.
- Inter-State Postgraduate Medical Association of North America, Philadelphia, Oct. 31-Nov. 4. Dr. W. B. Peck, 27 East Stephenson St., Freeport, Ill., Managing Director.
- Omaha Mid-West Clinical Society, Omaha, Oct. 24-28. Dr. J. D. McCarthy, 107 South 17th St., Omaha, Secretary.
- Pacific Coast Society of Obstetrics and Gynecology, Los Angeles, Nov. 2-4. Dr. T. Floyd Bell, 400 29th St., Oakland, Calif., Secretary.
- Radiological Society of North America, Pittsburgh, Nov. 28-Dec. 2. Dr. Donald S. Childs, 607 Medical Arts Bldg., Syracuse, N. Y., Secretary.
- Southern Medical Empire, Secretary, Nov. 15-18. Mr. C. P. Loran, Secretary.
- Southern Surgical, Secretary, Nov. 15-18. Mr. C. P. Loran, Secretary.
- Southwestern Medical Association, El Paso, Texas, Secretary, Nov. 15-18. Mr. C. P. Loran, Secretary.
- Western Surgical Association, Omaha, Dec. 2-3. Dr. Albert H. Montgomery, 123 South Michigan Blvd., Chicago, Secretary.

Current Medical Literature

AMERICAN

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Titles marked with an asterisk (*) are abstracted below.

American Journal of Medical Sciences, Philadelphia

196: 305-460 (Sept.) 1938

- Late Results in Treatment of Amebic Abscess and Hepatitis of the Liver. P. W. Brown and C. H. Hodgson, Rochester, Minn.—p. 305.
- *The "Hematopoietic Principle" in the Diseased Human Liver. L. Schiff, M. L. Rich and S. D. Simon, Cincinnati.—p. 313.
- Consideration of Phenomenon of Purpura Following Scarlet Fever. M. J. Fox and N. Enzer, Milwaukee.—p. 321.
- Chronic Leukemia: Study of Incidence and Factors Influencing Duration of Life. B. S. Leavell, New York.—p. 329.
- Failure of Electromagnetically Induced Heat to Increase Renal Efficiency. E. Blatt, P. J. Fouts and I. H. Page, Indianapolis.—p. 340.
- *Chemotherapy of Types VII and III Pneumococcus Infections with Sulfanilamide, 4,4'-Di-(Acetylaminio)-Diphenylsulfone and 4,4'-Diaminobenzene-sulfonanilide. F. B. Cooper, P. Gross and M. Lewis, Pittsburgh.—p. 343.
- Studies on Liver Function in Pneumococcal Pneumonia. T. J. Curphey, Garden City, N. Y., and S. Solomon, New York.—p. 348.
- Note on Rapid Desensitization in Case of Hypersensitiveness to Insulin. A. C. Coreoran, Indianapolis.—p. 359.
- Semen Analyses of 200 Fertile Men. R. S. Hotchkiss, E. K. Brunner and P. Grenley, New York.—p. 362.
- Vitamin C in the Spinal Fluid. H. Wortis, J. Liebmman and S. B. Wortis, New York.—p. 384.
- Note on Lack of Correlation of Capillary Fragility with Vitamin C Content of Blood, Spinal Fluid and Urine. J. Liebmman, H. Wortis and Ethel Wortis, New York.—p. 388.
- Note on Lack of Hemoregulatory Effect of Ascorbic Acid on Patients with Polycythemia Vera. E. V. Kandel and G. V. LeRoy, Chicago.—p. 392.
- Relief of Anginoid Pain Following Removal of Intrathoracic Nontoxic Nodular Goiter. J. Edeiken and E. Rose, Philadelphia.—p. 395.
- Isolated-Calcified Aortic Stenosis, with Particular Reference to Its Etiology and Differential Diagnosis. W. F. Friedewald, St. Louis, and A. R. Ewing, Philadelphia.—p. 400.
- Varieties of Single Coronary Artery in Man, Occurring as Isolated Cardiac Anomalies. E. B. Krumphaar and W. E. Ehrlich, Philadelphia.—p. 407.
- *Anemia of Alcohol Addicts: Observations as to Role of Liver Disease, Achlorhydria, Nutritional Factors and Alcohol on Its Production. A. Bianco and N. Jolliffe, New York.—p. 414.
- Convulsive (Pentamethylenetetrazol) Shock Therapy in Depressive Psychoses: Preliminary Report of Results Obtained in Ten Cases. A. E. Bennett, Omaha.—p. 420.

"Hematopoietic Principle" in Diseased Human Liver.—Schiff and his associates sought additional data on the presence (or absence) of the antianemic substance in the diseased human liver. The patients selected for injection had typical pernicious anemia with a red cell count between 1 and 3 million per cubic millimeter, had received no antianemic treatment in the form of liver, iron, arsenic or transfusions for at least one month prior to the injection, were free of infection (with one exception) and subsequently showed a complete remission under specific treatment. Before extracts of human livers were prepared, a control extract was made from a normal calf's liver and administered intramuscularly to a patient with pernicious anemia. A satisfactory response was obtained. Extracts were then prepared from the livers of five patients with hepatic disease. The extracts were then administered intramuscularly to the patients with pernicious anemia in relapse. A characteristic reticulocytosis resulted, followed by an increase in hemoglobin and red cell count and by definite clinical improvement. The three patients with cirrhosis presented a macrocytic anemia, while the type of anemia in the remaining two patients was not definitely determined. The conclusion is that the human liver may contain the specific hemopoietic principle even when it is the seat of extensive and protracted disease. This holds true even in the presence of macrocytic anemia and strongly suggests that the macrocytic anemia associated with hepatic disease is not caused by failure of the liver to store the specific antianemic substance.

Pneumococcal Infections and Sulfanilamide.—Cooper and his colleagues found 4,4'-di-(acetylaminio)-diphenylsulfone less effective than sulfanilamide against pneumococcal infections in mice caused by type VII and III strains, as well as in pneumococcal pneumonia in rats caused by the type III strain. The results reported, although at variance with those of other investigators, probably find explanation in differences of strain susceptibility to chemotherapy. Although 4,4'-diaminobenzene-sulfonanilide was at times more effective than sulfanilamide against the particular pneumococcus strains tested, it appears to be too toxic to warrant clinical trial. To the infectious caused by types I, II, III and XIV pneumococci which have previously been found susceptible to therapy by certain sulfonamide and sulfone compounds may be added those caused by the type VII pneumococcus. These experiments verify previous chemotherapeutic results in pneumococcal infections, namely that little or no protection in mice may be demonstrated against more than 100 fatal doses, whereas good protection has been repeatedly reported against ten fatal doses.

Anemia of Alcohol Addicts.—Bianco and Jolliffe carried out quantitative studies of the erythrocytes in 184 instances of addiction to alcohol. Of these subjects, 159 in addition to alcoholism had one or more of the following diseases: polyneuritis, pellagra, "alcoholic" stomatitis, "alcoholic" encephalopathy or cirrhosis of the liver. Quantitative anemia did not occur in the "uncomplicated" group of twenty-five subjects but was present in 61 per cent of the "complicated" group. Macrocytosis was present in about 50 per cent of both groups. Macrocytic anemia in these addicts to alcohol was not limited to subjects manifesting pellagra or cirrhosis of the liver but occurred as well, and in about the same frequency, in subjects having polyneuritis, "alcoholic" stomatitis and "alcoholic" encephalopathy. There was no correlation between the frequency of macrocytosis and achlorhydria, severity of hepatic damage or the presence of an enlarged liver. The macrocytosis of the addict to alcohol is not regarded as a manifestation of inability on the part of the liver to store a hemopoietic principle but as an extrinsic deficiency of some necessary hemopoietic substance required to maintain normocytosis.

American Journal of Public Health, New York

28: 1029-1152 (Sept.) 1938

- Health Hazards in the Dry Cleaning Industry: Preliminary Report of Survey of Dry Cleaning Establishments in the Detroit Metropolitan Area. W. H. Cary Jr., Detroit, and J. M. Hepler, Lansing, Mich.—p. 1029.
- Methods of Estimating Postcensal Populations. H. S. Shryock Jr., Princeton, N. J.—p. 1042.
- Handicaps in the Normal Growth and Development of Rural Negro Children. H. A. Poindexter, Washington, D. C.—p. 1048.
- Critical Discussion of Some Methods and Standards for Certified Milk. J. H. Brown, Baltimore.—p. 1053.
- More Effective School Health Program. J. T. Phair, Toronto.—p. 1059.
- Cultural Methods for Detection of Typhoid Carriers. Elizabeth J. Cope and J. A. Kasper, Detroit.—p. 1065.
- Present Status of Vitamin Milks. E. V. McCollum, Baltimore.—p. 1069.
- Postgraduate Education of Physicians in Pediatrics. M. E. Wegman, Baltimore.—p. 1072.
- What Every Health Officer Should Know: Vital Statistics. Jessamine S. Whitney, New York.—p. 1077.
- Id.: Industrial Hygiene. L. D. Bristol, New York.—p. 1080.
- Id.: Health Education. Mary P. Connolly, Detroit.—p. 1083.
- Id.: Public Health Nursing. Naomi Deutsch, Washington, D. C.—p. 1087.
- Federal Facilities to Expedite Emergency Sanitation Measures. R. E. Tarbell, Washington, D. C.—p. 1091.
- *Scarlet Fever Control. E. R. Krumbiegel, Milwaukee.—p. 1096.

Scarlet Fever Control.—Krumbiegel states that on March 12, 1934, the Milwaukee health department adopted the procedure of the Scarlet Fever Committee for Dick testing persons more than 18 months of age, and the subsequent immunization of those showing a positive reaction. In 1934 15,642 Dick tests were given, of which 10,500 were positive. Among these Dick positive reactors 1,769 received no toxin for immunization, while 6,497 received in 1934 either a standard five dose course or as many doses as they elected to receive. None of these subsequently received any artificial immunization. The fifth dose of toxin was received by 3,914 persons, of whom 3,532 were retested and appeared for reading. Of these, 240 were positive and 183 received a sixth dose of toxin. All cases have been followed through March 12, 1937. During

the three years the case rate for scarlet fever was more than fourteen times higher in the unimmunized Dick positive reactors than in those who completed the standard five dose course of toxin. During the three years the immunity derived from four doses of toxin was as effective as that from five doses. The case rates for scarlet fever were lower in primarily negative Dick reactors and positive reactors who completed the standard five dose course of toxin than for those who previously had an attack of scarlet fever. During the three years the practical value of retesting has proved negligible. A culture filtrate free of, or as near as possible free of, endotoxin is desirable, at least for the purpose of cutaneous testing.

Am. J. Syphilis, Gonorrhea and Ven. Dis., St. Louis

22: 537-668 (Sept.) 1938

- Present Status of Epidemiology of Gonorrhea. R. A. Vonderlehr and Lida J. Usilton, Washington, D. C.—p. 537.
- Prenatal Syphilis in One of Twins: Case Report. U. J. Wile and D. G. Welton, Ann Arbor, Mich.—p. 544.
- Clinical Excretion of Bismuth: VII. Autopsy Distribution of Bismuth in Patients After Clinical Bismuth Treatment. T. Sollmann, H. N. Cole and Katharine Henderson, with collaboration of G. W. Binkley, H. Connors, H. Reichle and D. Secof, Cleveland.—p. 555.
- Sources of Infection in Syphilis. G. V. Kulchar and Erla I. Ninnis, San Francisco.—p. 584.
- Yearly Admissions of Four Genito-Infectious Diseases at Cleveland City Hospital, with Special Reference to Syphilis. G. W. Binkley, Cleveland, and E. A. Levin, San Francisco.—p. 588.
- Prevention and Treatment of Neurosyphilis by Combined Artificial Fever and Chemotherapy: Report of Results in Seventy-Two Cases of Asymptomatic and Clinical Neurosyphilis. A. E. Bennett and M. D. Lewis, Omaha.—p. 593.
- *Acquired Syphilis of Infancy and Childhood: Report of Thirty-Five Cases. J. R. Waugh, Norfolk, Va.—p. 607.
- Syphilis Control in a Chemical Industry. G. H. Gehrman, Wilmington, Del.—p. 623.
- Ecthyma of Vulva Simulating Condyloma Latum. H. M. Robinson, Baltimore.—p. 631.
- Chancroidal Infection in the Female. R. Torpin and R. B. Dienst, Augusta, Ga.—p. 634.
- *Intravenous Aldarsone in Treatment of Neurosyphilis. G. R. Kamman, St. Paul.—p. 638.

Acquired Syphilis of Infancy and Childhood.—Waugh examined thirty-five infants and children with acquired syphilis, not prenatal syphilis, over a period of six years during which time there were admitted to the same service 183 cases of prenatal syphilis and 20,567 adult cases. Since the number of infants and children with syphilis admitted to this clinic is small compared to the number of adults, it would appear that the incidence of acquired syphilis of infancy and childhood may be considerably greater than generally recognized. Twenty-two children were between the ages of 5 months and 10 years, and two were 11 years of age. Only two of these infants (Negroes) acquired syphilis through definite sexual contact with other children or each other. Another white girl may have acquired her infection through sexual contact, although this was denied, since she had a genital chancre. Her mother also had syphilis. The source of infection in the case of the twenty-one other children was undoubtedly a parent, brother or sister. The other eleven children who were from 12 to 14 years of age acquired syphilis definitely through sexual intercourse. Two of these children (female) were married. All of these children were sexual delinquents except one of the two married girls. The manifestations of acquired syphilis in infants and children are the same as those in the adult. Fournier states that the primary adenopathy is less marked than in the adult. Severe anemia may accompany the secondary manifestations. Later sequelae have been severe and tertiary lesions have been common, caused probably by insufficient treatment. Arspenamine, neosphenamine and bismuth compounds were used intensively in the treatment of these infants and children, exactly as in the case of acquired syphilis in adults, except that the dosages were graduated according to age and weight. They tolerated anti-syphilitic treatment better than adults, there being no severe reactions and few mild reactions. The lesions disappeared and the children responded in every way as well as adults.

Intravenous Aldarsone in Neurosyphilis.—Kamman gave fifty-three patients with neurosyphilis 1,495 injections of the formaldehyde sulfoxylate of 3-amino-4-hydroxyl-phenylarsonic acid (aldarsone). The drug is dissolved in 10 cc. of sterile

distilled water and a beginning dose of 0.25 Gm. is given intravenously. It is then given at weekly intervals, the dose being raised to 0.5 Gm. the second week and to 1 Gm. the third week. Unless contraindicatory symptoms appear, twenty-four weekly injections are given, further treatment being determined by the clinical and serologic response. Forty of the fifty-three patients had received previous treatment with varying results. Clinically eleven of these patients had not improved under previous treatment but improved under aldarsone, eleven improved under previous treatment but did not show any further improvement under aldarsone, twelve improved under previous treatment and showed further improvement on aldarsone, five did not improve on previous treatment or on aldarsone, and four asymptomatic patients did not show clinical signs but there was definite serologic improvement. Serologically, thirteen patients did not improve on previous treatment but showed improvement on aldarsone, ten improved on previous treatment but did not improve further on aldarsone, ten improved under previous treatment and improved further on aldarsone, and five did not improve under either treatment. The serologic results in two patients are unknown. In four patients with tabes dorsalis the serologic and clinical improvement was accomplished by aldarsone alone. Toxic reactions definitely due to aldarsone were encountered in only three patients, and in only one patient was treatment discontinued because of toxic reactions. In no patient was it necessary to suspend treatment because of changes in the visual fields or in the optic disks. In three patients originally contracted fields enlarged under aldarsone, and in two others the contraction of the fields increased somewhat under aldarsone.

American Review of Tuberculosis, New York

38: 277-398 (Sept.) 1938

- *Results of Artificial Pneumothorax: Review of 530 Cases. G. F. Aycock and P. E. Keller, Denver.—p. 277.
- Lobectomy and Thoracoplasty in the Same Patient: Report of Three Cases. R. H. Overholt and R. H. Betts, Brookline, Mass.—p. 292.
- Healing of Experimental Pulmonary Tuberculosis by Fascial Transplantation and Bronchial Ligation. L. Escudero and W. E. Adams, Chicago.—p. 298.
- Disease of Accessory Nasal Sinuses: Its Incidence in a Tuberculosis Sanatorium. B. L. Brock, Waverly Hills, Ky., and J. C. Bell, Louisville, Ky.—p. 312.
- Bronchial Occlusion Due to Tuberculous Lymphadenitis. L. V. Schneider, Glenn Dale, Md.—p. 320.
- Anemia as a Predisposing Factor in Tuberculosis. Cecilia Shiskin and S. R. Gloyne, Victoria Park, England.—p. 325.
- Pathogenesis of Tuberculosis in Children. H. S. Willis, Northville, England.—p. 336.
- Influence of Silica on Natural and Acquired Resistance to Tubercle Bacillus. A. J. Vorwald and A. B. Delahant, Saranac Lake, N. Y.—p. 347.
- Pathology of the Silicotic Nodule. J. Walsh, Philadelphia.—p. 363.
- Sedimentation Rate of Red Blood Cells in Plasma, Pleural and Aqueous Fluids. S. Cohen, P. Faraci and B. S. Pollak, Jersey City, N. J.—p. 372.
- *Prontosil in Experimental Tuberculosis: Preliminary Report. H. F. Dietrich, Beverly Hills, Calif.—p. 388.
- Influences of Mycetes on Tubercle Bacilli: Preliminary Report. D. Barglowski, Pueblo, Calif.—p. 393.

Results of Artificial Pneumothorax.—Aycock and Keller analyze the results of 530 cases of artificial pneumothorax essentially on the basis of the reactions of the dominant tissue at the time artificial pneumothorax was induced in each case. These reactions were considered under three general groups. Exudative, caseous pneumonic and fibrocavernous. Satisfactory results were obtained in 301 cases. In the exudative group alone there were 250 cases; satisfactory results were obtained in 73.5 per cent. The incidence of important complications, such as pleural exudate and superimposed spontaneous pneumothorax, was highest in the fibrocavernous group. The high percentage of satisfactory results from artificial pneumothorax in the exudative cases simply means that this is the optimal phase in which to apply this form of therapy. In this phase the mechanical barriers resulting from the fibrosis incident to healing and tissue replacement have not become dominant. Accordingly, satisfactory collapse is obtained more readily. On the other hand, the fibrocavernous group comprises cases in the healing or reparative phase. Fibrosis has become the dominant tissue reaction and as a result certain mechanical barriers have been formed, which threaten the successful issue of artificial pneumothorax. The caseous pneumonic group represents cases in a

sort of intensified exudative phase. The number of such cases reviewed is too small to serve as a basis for definite conclusions as to the results of collapse therapy.

Prontosil in Experimental Tuberculosis.—Dietrich chose the disodium salt of 4-sulfamido-phenyl-2'-azo-7'-acetyl-amino-1'-hydroxynaphthalene-3',6'-disulfonic acid (prontosil) in a 2.5 per cent solution for its effect on experimental tuberculosis in the guinea pig. Six animals were given 0.5 cc. of a suspension of tubercle bacilli recovered from the lung of a patient dying of tuberculosis and four were injected with 0.25 cc. of the suspension. All inoculations were made subcutaneously just cephalad to the right groin. The prontosil administered was injected into the peritoneal cavity in single daily doses of 100 mg. per kilogram of body weight. No animal showed any peritoneal reaction to the injected prontosil. Treated animals died much sooner than did the untreated controls. The pathology of tuberculosis offers an excellent reason why, even if one possessed an agent strongly bactericidal for the tubercle bacillus in vitro, the bacilli might be unaffected in experimental and clinical infections. Prontosil did not inhibit the growth or spread of tubercle bacilli, even though it came in contact (by prontosil being given before inoculation with tubercle bacilli) with them before they were fixed in the tissues.

Archives of Neurology and Psychiatry, Chicago

40: 417-638 (Sept.) 1938

- Cerebral Cortex in Man: I. Cerebral Cortex and Consciousness. W. Penfield, Montreal.—p. 417.
Sweat Secretion in Man: IV. Sweat Secretion of the Face and Its Disturbances. C. F. List and M. M. Peet, Ann Arbor, Mich.—p. 443.
Quantitative Olfactory Tests: Value in Localization and Diagnosis of Tumors of the Brain, with Analysis of Results in 300 Patients. C. A. Elsberg and Jane Stewart, New York.—p. 471.
Margins of Optically Excitable Cortex in the Rabbit. J. L. O'Leary and G. H. Bishop, St. Louis.—p. 482.
Effect of Lesions in Vestibular Part of Cerebellum in Primates. R. S. Dow, New Haven, Conn.—p. 500.
Acute Amaurotic Epilepsy in Macacus Rhesus. L. van Bogaert and H. J. Scherer, Antwerp, Belgium.—p. 521.
Negation or Reversal of Legal Testimony. M. H. Erickson, Eloise, Mich.—p. 548.
Dermoid of Spinal Cord: Report of Case in Which There Was Removal with Improvement. C. B. Masson, New York.—p. 554.
Modifications in Technic for Use of Horsley-Clarke Stereotaxic Instrument. F. Harrison, Chicago.—p. 563.

Archives of Pathology, Chicago

26: 603-764 (Sept.) 1938

- Giant Follicular Lymphadenopathy With or Without Splenomegaly: Its Transformation into Polymorphous Cell Sarcoma of the Lymph Follicles and Its Association with Hodgkin's Disease, Lymphatic Leukemia and an Apparently Unique Disease of the Lymph Nodes and Spleen—a Disease Entity Believed Heretofore Undescribed. D. Symmers, New York.—p. 603.
*Histology of Bone Marrow in Aplastic Anemia. C. P. Rhoads and D. K. Miller, New York.—p. 648.
Incidence of Mild Degrees of Atrophy in Fasciculus Gracilis. D. Duncan, Galveston, Texas.—p. 664.
Systemic Proliferation of Reticulo-Endothelial System (Reticulo-Endotheliosis): Report of Case and Comments on the Literature. M. S. Sacks, Baltimore.—p. 676.
Attraction of Human Polymorphonuclear Leukocytes by Tuberculo-protein. W. B. Wartman, Cleveland.—p. 694.
Metchnikoff's Contribution to Pathology. B. M. Fried, New York.—p. 700.

Bone Marrow in Anemia.—Rhoads and Miller studied the living cells of the sternal marrow by the supravital technic of Sabin in forty-one cases of aplastic anemia. On the basis of the histologic changes observed in the stained preparations, it is possible to divide the cases into five general groups: aplastic anemias with aplastic, hyperplastic (pluricytopenia), active, megakaryocytic or sclerotic marrows. The basic change common to the aplastic, active and hyperplastic subgroups was a failure of maturation of the hemopoietic cells at an early, undifferentiated stage. Comparison of marrow from persons presenting aplastic anemia with marrows from persons presenting acute agranulocytosis shows in the latter a similar lack of maturation and suggests that aplastic anemia and acute agranulocytosis may have some etiologic factor in common. Although a defect in maturation is present in the megakaryocytic group, the major change is a replacement of hemopoietic marrow by a cellular structure made up of megakaryocytes and their precursors. The sclerotic group is characterized by an elongation and matting together of the marrow cells.

Archives of Surgery, Chicago

37: 353-520 (Sept.) 1938

- *Fantom Limb Pain: Report of Ten Cases in Which It Was Treated by Injections of Procaine Hydrochloride Near Thoracic Sympathetic Ganglions. W. K. Livingston, Portland, Ore.—p. 353.
Osteomyelitis of the Pelvic Girdle. A. O. Wilensky, New York.—p. 371.
Studies of Hepatic Function by Quick Hippuric Acid Test: I. Biliary and Hepatic Disease. F. F. Boyce and Elizabeth M. McFetridge, New Orleans.—p. 401.
Id.: II. Thyroid Disease. F. F. Boyce and Elizabeth M. McFetridge, New Orleans.—p. 427.
Id.: III. Various Surgical States. F. F. Boyce and Elizabeth M. McFetridge, New Orleans.—p. 443.
*Treatment of Intractable Bronchial Asthma by Bilateral Resection of Posterior Pulmonary Plexus. W. F. Rienhoff Jr. and L. N. Gay, Baltimore.—p. 456.
Behavior of Joint Cartilage in Late Rickets: Contribution to Question of Atrophy of Cartilage. E. Freund, Los Angeles.—p. 470.
Treatment of Postoperative Parathyroid Insufficiency with Dissolved Calcium Lactate. S. J. Wilson, Columbus, Ohio.—p. 490.
Mechanical Intestinal Obstruction Complicating Pelvic Inflammatory Disease. M. H. Levine and G. Blinick, New York.—p. 498.
Tuberculosis of the Stomach. O. T. Clagett and W. Walters, Rochester, Minn.—p. 505.

Fantom Limb Pain.—In his capacity as medical examiner for the state industrial accident commission of Oregon, Livingston has examined a number of men who have had an upper extremity amputated. The proportion of these who feel pain in the fantom limb is surprisingly high, and the similarity in their complaints is so striking as to warrant the term "fantom limb pain syndrome." Ten cases are reported. In all of these the patients have had one or more injections of procaine hydrochloride near the thoracic sympathetic ganglions of the affected side. Eight patients felt immediate relief from pain, together with an extraordinary sequence of subjective and objective changes. In four of these the relief was of sufficient degree and duration to suggest that injection of procaine hydrochloride is of therapeutic value. The pain syndrome and its implications in relation to the general problem of pain are discussed.

Resection of Posterior Pulmonary Plexus in Asthma.—The rationale of the procedure of bilateral resection of the posterior pulmonary plexus is based on the anatomic fact that only at this point can the extrinsic nerve supply of the lung be completely interrupted. By resection of this plexus it is therefore possible to isolate the entire organ from any influence brought to bear on the lung through its extrinsic nerve supply. The selection of patients for this method of treatment depends on the severity and frequency of the asthmatic seizures. The eleven patients that Rienhoff and Gay chose for the treatment were repeatedly in an asthmatic condition before operation and were consequently economically and socially incapacitated. The first patient was operated on in March 1934 and the last in March 1936. Five additional patients have been operated on since March 1936, three of whom at the time of writing have remained completely well for one year and two of whom remain improved after a shorter period. Deaths which could be attributed to the operative procedure have not occurred. Convalescence has been uneventful, with one exception: the patient, an elderly Negro, died several weeks after the second stage of the operation had been completed. The patient had suffered for years from asthmatic seizures associated with a high degree of arteriosclerosis, hypertension and some chronic myocardial change. Of the ten patients discharged from the hospital, one was entirely unimproved; one improved for three months, finally dying of what seemed to be cardiac failure; four are completely well at the time of writing, having been free of attacks since operation or a short time later, and have been able to resume their former work, and four have occasional mild attacks of asthma, all of which are controlled by small doses of ephedrine.

Bulletin New York Academy of Medicine, New York

14: 521-582 (Sept.) 1938

- Experimental Hypertension Induced by Renal Ischemia (Harvey Lecture, May 19, 1938). H. Goldblatt, Cleveland.—p. 523.
Endoscopic Prostatic Resection. J. F. McCarthy, New York.—p. 554.
*Specific Prevention of Diphtheria: Further Observations and Inquiries. J. G. FitzGerald, D. T. Fraser, N. E. McKinnon and M. A. Ross, Toronto.—p. 566.

Specific Prevention of Diphtheria.—FitzGerald and his colleagues state that prior to the use of toxoid there was no effectual control of diphtheria in Canada. In spite of the free distribution of antitoxin for prevention as well as for treatment,

recorded diphtheria morbidity persisted at its previous high levels and the mortality, though falling, still presented one of the most important public health problems. The reaction test, as devised by Moloney, practically obviated the hazard of reactions and thus facilitated the wide use of toxoid. Requirements for the Selick test are in need of revision and standardization. It is not infallible and its limitations should be recognized. Titrations of the blood serum of children who initially had no antitoxin and were then submitted to various immunization procedures show that three doses of unmodified diphtheria toxoid induced a higher antitoxin response than any of the other procedures compared (two doses of unmodified diphtheria toxoid, one dose of alum precipitated toxoid and two doses of alum precipitated toxoid). Titrations of blood serum of vaccinated children indicate a loss in antitoxin as time passes. Field studies show that the reduction in diphtheria, in those vaccinated with two doses of toxoid is, like the antitoxin response, less than the reduction in those vaccinated with three doses, and that the diphtheria occurring in the latter group is reduced by approximately 90 per cent as compared with that found in schoolmates under the same exposure. Records show striking declines in diphtheria morbidity and mortality and in the incidence of carriers in various cities and provinces in Canada following the wide use of toxoid, leaving no doubt that the decline is due to immunization. The extent of the decline in several of the large cities and in certain of the provinces of Canada shows indubitably that diphtheria is a preventable disease.

Connecticut State Medical Society Journal, Hartford

2: 423-476 (Sept.) 1938

- Submarine Escape Training. A. S. Chrisman, New London.—p. 423.
Physicians and Lawyers. G. H. Cohen, Hartford.—p. 431.
Syphilis of the Central Nervous System. G. A. Gosselin, Hartford.—p. 435.
The Preschool Age: The Stepchild in Preventive Medicine. S. A. Rose, Stamford.—p. 439.
Surgical Treatment of Peptic Ulcer. T. J. Sullivan, New Haven.—p. 441.
Connecticut Obstetric Consulting Service. J. H. Howard, Bridgeport.—p. 443.

Endocrinology, Los Angeles

23: 121-262 (Aug.) 1938

- *Effect of Testosterone Propionate on Genitalia, Prostate, Secondary Sex Characters and Body Weight in Eunuchoidism. A. T. Kenyon, Chicago.—p. 121.
Effect of Testosterone Propionate on Nitrogen, Electrolyte, Water and Energy Metabolism in Eunuchoidism. A. T. Kenyon, Irene Sandiford, A. H. Bryan, Kathryn Knowlton and F. C. Koch, Chicago.—p. 135.
Effect of Gonadotropic Hormones on Persisting Corpora Lutea in Hypophysectomized Rats. R. O. Green, Cambridge, Mass.—p. 154.
Gonadotropic Action of Normal Male Urine Extract on Dog. J. H. Leatham and J. A. Morrell, Princeton and New Brunswick, N. J.—p. 164.
Effect of Castrate Urine Hormone on Testis. H. S. Rubinstein, Baltimore.—p. 171.
Adiposity and Diabetes Mellitus in a Monkey with Hypothalamic Lesions. S. W. Ranson, C. Fisher and W. R. Ingram, Chicago.—p. 175.
Miscellaneous Experiments on Estrogen-Progesterone Induction of Heat in Spayed Guinea Pig. J. L. Boling; W. C. Young, Providence, R. I., and E. W. Dempsey.—p. 182.
Quantitative Studies of Experimentally Induced Sexual Receptivity in Spayed Guinea Pig. V. J. Collins, J. L. Boling, E. W. Dempsey and W. C. Young, Providence, R. I.—p. 188.
Partial Inhibition of Sex Activity in Intact Female Rat by Injected Estrin. Josephine Ball, Baltimore.—p. 197.
Histologic Effects Induced in Anterior Pituitary of Rat by Prolonged Injection of Estrin with Particular Reference to Production of Pituitary Adenomas. J. M. Wolfe, Nashville, Tenn., and A. W. Wright, Albany, N. Y.—p. 200.
Cellular Changes in Anterior Hypophyses of Vitamin A Deficient Rats. T. S. Sutton and B. J. Brief, Columbus, Ohio.—p. 211.
Postadrenalectomy Diuresis: Effects of Cortical Extracts, Salts and Estrone. R. Gaunt, H. E. Potts and Eleanor Loomis, New York.—p. 216.
Response to Cold Following Double Adrenalectomy. S. M. Horvath, Columbus, Ohio.—p. 223.
Are the Lactogenic and Carbohydrate Metabolism Hormones Identical? A. J. Bergman and C. W. Turner, with technical assistance of P. T. Cupps, Columbia, Mo.—p. 228.
Fatty Atrophy Following Insulin Injection in Nondiabetic Malnutrition. H. Blotner, Boston.—p. 233.

Testosterone Propionate and Eunuchoidism.—Kenyon gave four eunuchs subcutaneous injections of 25 mg. of testosterone propionate in sesame oil daily. The injections were given from five to seven times a week for from twenty-eight to ninety-nine days. Thereafter, in three of these, from 10 to 25 mg. was given from three to seven times a week. with

interruptions, until the one hundred and eighth to the one hundred and sixty-third day. There was an early increase in erections in the four eunuchs, in three an enlargement of the penis, in all an enlargement of the prostate, in two a distinct deepening of the voice and in three an increase in sexual hair. Hypertrophy of the tissue of the breast occurred in one patient, the size of the testes was unaltered in the two patients studied, but the sperm disappeared during treatment in one of these two, to reappear later. In all four patients there was an increase in body weight, in two accompanied by increased appetite and in two by evident edema. In one there was a slight increase in the basal metabolic rate.

Indiana State Medical Assn. Journal, Indianapolis

31: 433-536 (Sept.) 1938

- Incidence and Prevalence of Diseases of the Heart. H. Emerson, New York.—p. 433.
Quantity and Quality of Life. R. L. Sensenich, South Bend.—p. 437.
Prognosis in Bundle Branch Block. G. S. Bond and C. S. Campbell, Indianapolis.—p. 440.
The Psychoneurotic in the General Practice of Medicine. K. A. Menninger, Topeka, Kan.—p. 442.
Ovarian Dysfunctions: Management: Aids to Diagnosis. W. E. Herrell, Rochester, Minn.—p. 445.
Smallpox. F. Dragoo and R. D. Arford, Middletown.—p. 451.
Peptic Ulcer: Present Status of Its Management. A. E. Mable, Chicago.—p. 452.

Johns Hopkins Hospital Bulletin, Baltimore

63: 129-208 (Sept.) 1938

- Prognosis in Cases of Tuberculosis of Tonsils, Adenoids and Cervical Lymph Nodes: Study of Patients Followed for Eleven to Twenty-Three Years. J. Bordley 3d and J. W. Baylor, Baltimore.—p. 122.
Dietary Protein and Regeneration of Serum Albumin: I. Method of Assay and Discussion of Principles. A. A. Weech and E. Goettlich, New York.—p. 154.
Id.: II. Comparison of Potency Values of Beef Serum, Beef Muscle and Casein. A. A. Weech and E. Goettlich, New York.—p. 181.
Intracardiac Tumor Producing Signs of Valvular Heart Disease. C. W. Wainwright, Baltimore.—p. 187.

Journal of Bacteriology, Baltimore

36: 111-222 (Aug.) 1938

- *Degeneration and Variation of Gonococci. W. A. Casper, New York.—p. 111.
Studies on Hemolytic Streptococci: V. Characteristics of Human and Animal Strains of Groups A and C. Alice C. Evans and Elizabeth Verler, Washington, D. C.—p. 133.
Nutrient Requirements of *Lactobacillus Delbrückii* in Lactic Acid Fermentation of Molasses. H. R. Stiles and L. M. Pruess, Terre Haute, Ind.—p. 149.
Absorption of Staphylococcus Bacteriophages by Enterococci. M. L. Rakiety and E. J. Tiffany, Brooklyn.—p. 155.
Microbiology of the Upper Air: III. Improved Apparatus and Technique for Upper Air Investigations. B. E. Proctor and B. W. Parker, Cambridge, Mass.—p. 175.
Colchicine Stimulation of Yeast Growth Fails to Reveal Mitosis. Q. W. Richards, New Haven, Conn.—p. 187.
Simple Method for Sterile Filtration of Small Amounts of Fluid. I. Y. Asheshov, London, Ont.—p. 197.
Nutrition of Propionic Acid Bacteria. H. G. Wood, A. A. Andersen and C. H. Werkman, Ames, Iowa.—p. 201.

Degeneration and Variation of Gonococci.—Casper states that strains of gonococci from fresh cases of acute gonorrhea in the male and classified as two distinct serological types were transformable from the papilla-bearing to the papilla-free form. The formation of papilla-free colonies is a sign of degeneration probably due to growth on artificial mediums. Diagnostic serums prepared with such degenerated cultures are likely to give rise to errors in classification. Classification based only on colony morphology does not serve to exclude the possibility that one may be dealing not with different types of gonococci but with degenerated forms of the same type which have lost only their type specific carbohydrate. Associated with the loss of carbohydrate in old gonococcus cultures there is a developing relationship between formerly heterologous strains. Since, at the time of isolation of gonococci from acute cases of gonorrhea, one cannot estimate the degree of their degeneration, this fact may explain the relatively high frequency of overlapping strains. In chronic gonorrhea the gonococcus, by adaptation to the human tissue may undergo the same degenerative processes that occur after prolonged cultivation on artificial mediums. After cultivation on artificial mediums, strains of gonococci which were type specific in the comparative agglutination test were shown by slide agglutination to have mixed-phase colonies.

Journal of Clinical Investigation, New York

17: 539-698 (Sept.) 1938

- President's Address: Clinical Epidemiology. J. R. Paul, New Haven, Conn.—p. 539.
- Calcium and Phosphorus Metabolism in Diseases of Thyroparathyroid Apparatus: II. Calcium and Phosphorus Balance (A) Following Therapeutic Radiation of Hyperplastic Thyroid Gland and (B) in Hyperthyroid Patients Treated with Iodine. F. S. Hansman, with statistical analysis by W. A. C. Fraser, Sydney, Australia.—p. 543.
- Study of Tendency to Edema Formation Associated with Incompetence of Valves of Communicating Veins of Leg: Oxygen Tensions of Blood Contained in Varicose Veins. H. E. Hollings, H. K. Beecher and R. R. Linton, Boston.—p. 555.
- Determination of Cardiac Output in Man at Brief Intervals by a Modification of Ethyl Iodide Method. J. C. Snyder, Boston.—p. 563.
- Cardiac Output and Oxygen Consumption of Nine Surgical Patients Before and After Operation. J. C. Snyder, Boston.—p. 571.
- Measurements of Circulation in Constrictive Pericarditis Before and After Resection of Pericardium. H. J. Stewart, G. J. Heuer, J. E. Deitrick, N. F. Crane, R. F. Watson and C. H. Wheeler, New York.—p. 581.
- Renal Excretion at Low Urine Volumes and Mechanism of Oliguria. L. C. Chesley, Jersey City, N. J.—p. 591.
- *Value of Acid Test Meal: Study of Normal Persons and of Persons with Duodenal Ulcer. C. S. Welch and M. W. Comfort, Rochester, Minn.—p. 599.
- Placental Interchange: II. Comparison of Total Base Concentration of Fetal and Maternal Blood at Parturition. H. E. Thompson Jr. and W. T. Pommerenke, Rochester, N. Y.—p. 609.
- Attempt to Increase Resistance to Pertussis in Newborn Infants by Immunizing Their Mothers During Pregnancy. J. A. Lichty Jr., Betty Slavin and W. L. Bradford, Rochester, N. Y.—p. 613.
- Permanence of Recovery in Acute Glomerulonephritis. Emily Nichols Loeb, J. D. Lyttle, D. Seegal and Elizabeth L. Jost, New York.—p. 623.
- *Serum Antistreptolysin Titer in Acute Glomerulonephritis. J. D. Lyttle, D. Seegal, Emily Nichols Loeb and Elizabeth L. Jost, New York.—p. 631.
- Experience with the Hamilton and Highman Test for Parathyroid Hyperfunction in Chronic Nephritis, Toxic Goiter and Paget's Disease of Bone. D. R. Gilligan, Marie C. Volk and S. L. Gargill, Boston.—p. 641.
- Choline-Esterase Activity of Blood Serum in Disease. A. T. Milhorat, New York.—p. 649.
- Effect of Artificial Pneumothorax on Anoxemia of Pneumonia. D. Goldstein, M. Block and M. Rosenbluth, New York.—p. 659.
- Basal Gastric Secretion in Cases of Peptic Ulcer: Relation of Acidity to Healing of Ulcer. A. L. Bloomfield and L. R. French, San Francisco.—p. 667.
- *Requirements for Vitamin C in Man. M. Heinemann, New Haven, Conn.—p. 671.
- Use of Globulin Substance Derived from Beef Plasma as a Local Hemostatic in Hemophilia. F. J. Pohle and F. H. L. Taylor, Boston.—p. 677.
- Control of Renal Blood Flow and Glomerular Filtration in Normal Man. H. Chasis, H. A. Ranges, W. Goldring and H. W. Smith, New York.—p. 683.

Value of Acid Test Meal.—Welch and Comfort used the method evolved by Wilhelmj, Neigus and Hill in obtaining information concerning the relative amounts of acids and alkaline fluids that enter the stomach during the test meal. Twenty-five normal persons and thirty persons who had duodenal ulcer were tested. The test provided an excellent method for studying the factors that regulate acidity of the gastric contents and demonstrated the interplay of dilution and neutralization and of acid secretion. The method permits measurement of the reductions of the concentration of acid chloride in the test fluid during the test period, of the excess of acid or alkaline material in the combined fluids that enter the stomach and of the effectiveness of the factor of dilution. The method does not permit measurement of the total amount of acid secreted, of the total amount of alkali that enters the stomach or of the total neutralization of acid chloride during the test period. It demonstrates the effectiveness of duodenal regurgitation in reducing acidity of the gastric contents and that this reduction is attributable partly to dilution and partly to neutralization. Increased regurgitation of duodenal fluid has again been shown to be an effective means of reducing acidity of the gastric contents. Regurgitation increases the reduction attributable to both dilution and neutralization. The relative importance of the factors concerned in the regulation of acidity of the gastric contents is different in normal persons. The alkaline elements are greater than the acid elements in the fluids entering the stomachs of most normal persons, whereas the reverse holds true in patients who have duodenal ulcer. As a result of this fundamental difference, dilution tends to be 100 per cent effective in normal persons while this is rarely so in cases of duodenal ulcer. Neutraliza-

tion of the acid chloride of the test solution is usually measurable among normal persons but occurs rarely in duodenal ulcer. The acid secreted by the fundic cells appeared to have a greater average volume in cases of duodenal ulcer than it did in normal persons. While there is evidence that there is a relative deficiency of alkali in the fluid that enters the stomach of patients who have duodenal ulcer, the method does not permit a statement that there is an actual deficiency.

Serum Antistreptolysin in Glomerulonephritis.—Lyttle and his co-workers base their study on 116 consecutive and unselected patients with acute glomerulonephritis (ninety-five children less than 13 years of age and twenty-one adults). Many of the patients were admitted to the hospital because of the severity of an infection, and subsequently routine examination showed the presence of nephritis. The majority of patients showed definite clinical and bacteriologic evidence of hemolytic streptococcus infection but many gave only a vague or negative history of preceding infection. Most of the patients in the series showed evidence of infection of the upper part of the respiratory tract preceding or accompanying the onset of acute nephritis. The infection was located in the upper part of the respiratory tract or its appendages in 104 cases. In twelve the data were insufficient to make a clinical diagnosis. The maximal titer of antistreptolysin was usually reached in the first few weeks of the disease, which has its onset about two weeks following the acute infection. The highest antistreptolysin titer in the first forty days after the onset of the nephritis was shown in each case. In 94 per cent of 116 cases the antistreptolysin titer was above 125 units and in 27 per cent the titers were between 1,000 and 2,500 units. Since the authors consider 125 units to be the upper normal level of antistreptolysin, this lends further support to the results of direct culture and indicates that the great majority of patients with acute glomerulonephritis have had a recent hemolytic streptococcus infection. Careful study of the clinical and immunologic data indicate that in the acute stages of glomerulonephritis the maximal antistreptolysin titer (1) is not related to age or sex, (2) has no relation to the severity or duration of the nephritis but (3) is definitely related to the type and severity of the acute infection which precedes or accompanies the acute nephritis.

Vitamin C Requirements in Man.—The estimation of the daily requirements of vitamin C depends necessarily on the criteria applied. From a study of the literature Heinemann finds that at least 0.8 mg. of ascorbic acid per kilogram of body weight is used daily by a saturated normal subject. Smaller doses, e. g., 0.5 mg. or even less, are sufficient to protect a person against scurvy. But, even if it is true that smaller doses may assure good health under optimal conditions, it would seem useful to supply the maximal requirements as a factor of safety against altered circumstances which may increase requirements. An abnormally high supply seems to be needed in many diseases (tuberculosis, pneumonia, rheumatism), but this does not appear to be specific for any one disease. Requirements are unusually high in tuberculosis. Tuberculosis predisposes to scurvy by increasing the requirements for vitamin C. Amounts that will meet normal demands become inadequate. Abnormally increased requirements are not specific for tuberculosis, as studies in other diseases show. Requirements have been found to be increased to some extent in patients with peptic ulcer, in whom similar experimental data were obtained by either oral or subcutaneous administration of the vitamin. Saturation tests have revealed that deficiency of vitamin C is rather common in this group of patients, but in only a few cases has manifest scurvy been described.

Journal Industrial Hygiene & Toxicology, Baltimore

20: 457-496 (Sept.) 1938

- Method for Analysis of Dust and Fumes for Lead and Zinc. S. Moskowitz and W. J. Burke, New York.—p. 457.
- Gases from Carbon Arcs: Absence of Ozone. R. W. Colman and H. G. MacPherson, Cleveland.—p. 465.
- Chronic Nicotine Toxicity: IV. Effect of Nicotine-Containing Diets on Histology and Weights of Organs of Albino Rats. R. H. Wilson, J. B. McNaught and F. DeEds, San Francisco.—p. 468.
- Radiation as Factor in Heating Canadian Homes and in Body Heat Loss. Ruth C. Partridge and D. L. MacLean, Toronto.—p. 482.
- Effect of the Diet in Toxicologic Studies. I. A. Manville, F. J. Reithel and P. M. Yamada, Portland, Ore.—p. 492.

Journal of Investigative Dermatology Baltimore

1: 171-234 (June) 1938

- Studies in Contact Dermatitis: III. Active Sensitization with Krameria in Man. M. Grohnick, Brooklyn.—p. 179.
- Further Studies in Arspheamine Hypersensitiveness in Guinea Pigs: I. Cutaneous and Anaphylactic Responses to Old Arspheamine and to Neorspheamine After Sensitization with Old Arspheamine. W. Frei and M. B. Sulzberger, New York.—p. 191.
- Experimental Arspheamine Sensitization: Further Observations on Reactions to Arspheamine in Guinea Pigs Given Staphylococcus Toxin and in Guinea Pigs with Induced Streptococcal Infection. F. E. Cornia, Montreal.—p. 199.
- Investigation of Method for Preventing Dermatitis from Dress Shields. L. Schwartz and G. C. Andrews, New York.—p. 219.
- Effect of Copper in Vitiligo. B. Shaffer, Philadelphia.—p. 225.

Journal-Lancet, Minneapolis

58: 385-426 (Sept.) 1938

- Diagnosis and Office Treatment of Rectal Diseases. W. A. Fansler, Minneapolis.—p. 385.
- Uterine Surgical Problems in General Practice. V. S. Counseller, Rochester, Minn.—p. 388.
- The Doctor in Health Education. W. W. Bauer, Chicago.—p. 393.
- Medical Relief in North Dakota. E. A. Willson, Bismarck, N. D.—p. 395.
- What the General Practitioner Should Know About Insanity. L. J. Pankow, Sioux Falls, S. D.—p. 397.
- The Management of Abortion. J. H. Moore, Grand Forks, N. D.—p. 402.
- The Meaning of "Athletic Heart" Among University Athletes. D. G. Stine, Columbia, Mo.—p. 405.

Journal of Urology, Baltimore

40: 359-466 (Sept.) 1938

- Primary Sympathoblastoma of Left Adrenal with Extension into and Obstruction of Pelvic Cavity of Adjacent Kidney. S. E. Krohn and W. J. Kennedy, Gloversville, N. Y.—p. 359.
- Experimental Hydronephrosis in Dogs: I. Composition of Blood Serum. Lillian Eichelberger, with technical assistance of M. Roma, Chicago.—p. 366.
- Bilateral Torsion of the Ureter: Case Report and Brief Review of Literature. J. V. Berry, Ottawa, Ont.—p. 378.
- Uterovaginal Fistula Successfully Repaired by Combined Vaginal and Transvesical Operation. H. V. Findlay, Santa Barbara, Calif.—p. 384.
- Endometriosis of the Bladder: Report of Case. P. S. Adams, New York.—p. 390.
- Myositis Ossificans Following Suprapubic Prostatectomy. J. Schwartz, New York.—p. 397.
- Thrombophlebitis of Periprostatic Plexus. A. Hyman and H. Leiter, New York.—p. 403.
- Multiple Primary Cancers. H. L. Kretschmer, Chicago.—p. 421.
- *Diabetes in Surgical Urology. J. Duff and F. W. Williams, New York.—p. 446.
- Practical Cystometer. O. W. Davidson, Kansas City, Kan.—p. 452.
- Better Medical Writing: Some Typical Errors and How to Avoid Them. R. M. Hewitt, Rochester, Minn.—p. 454.
- Gangrene of Glans Penis and Urethra in a Diabetic. T. M. Townsend and W. M. Flagg, New York.—p. 464.

Diabetes in Surgical Urology.—Out of a total of 3,158 patients admitted to their urologic service during a period of five years Duff and Williams diagnosed thirty-nine as having diabetes. Seventeen of these patients were operated on. Such a patient, having undergone proper preoperative treatment, is no greater operative risk than the average well prepared non-diabetic patient. Occasionally emergency operative measures must be undertaken for a diabetic patient who has not received adequate preoperative treatment. In such a case an internist determines the proper dosage of insulin or sugar, or both. As a result of the study of diabetic surgical patients, provided the patient is not dehydrated and shows a minimum of sugar and no acetone in the urine, he is a good surgical risk, irrespective of the amount of sugar in the blood; as a matter of fact a moderately high blood sugar content is regarded as a surgical safety factor. Except for intense pain, there is practically no subjective symptom referable to the urinary tract which may not be of diabetic origin. Four of the diabetic patients died: one from coronary occlusion, two from sepsis and one from post-operative shock. Two patients not operated on died of uremia. There were no deaths directly attributable to diabetes. From the standpoint of the diabetes, there are only two contraindications to operation: marked dehydration and profound coma. These complications of diabetic origin are not encountered frequently, for the diabetes in the urologic age group is usually mild. A patient is considered ready for operation, from the

standpoint of his diabetes, if he is not clinically dehydrated, there is no ketosis and glycosuria is 1 per cent or less for twenty-four hours. In patients in profound coma, there must be a differential diagnosis between diabetic and uremic coma.

Kansas Medical Society Journal, Topeka

39: 325-368 (Aug.) 1938

- Cardiovascular Syphilis: Diagnosis and Therapy. A. Arkin, Chicago.—p. 325.
- Induced Nontoxic Jaundice (Hyperbilirubinemia) in Patients with Atrophic Arthritis: Second Report. H. E. Thompson and R. L. Wyatt, Tucson, Ariz.—p. 327.
- Cycloplegics, Mydriatics and Miotics. L. S. Powell, Lawrence.—p. 330.
- Tuberculin Survey of School Children in Sedgwick County. F. C. Beelman, Wichita.—p. 333.

Kentucky Medical Journal, Bowling Green

36: 349-408 (Sept.) 1938

- Production, History, Chemistry, Physics and Biologic Effects of Radium. D. Y. Keith, Louisville.—p. 387.
- Results of Radium Treatment of Carcinoma Cervix. J. Love, Louisville.—p. 391.
- Scientific Exhibits of the American Medical Association, San Francisco, June 1938. M. Casper, Louisville.—p. 398.
- The Transport of Carbon Dioxide in the Blood. H. Lawson, Louisville.—p. 401.

Laryngoscope, St. Louis

48: 527-614 (Aug.) 1938

- What Can Be Done for Chronic Progressive Deafness? (a) Study in Treatment of Deafness. C. S. Nash, Rochester, N. Y.—p. 527.
- Id.: (b) Rationale, Technique, Case Reports and Observations with Grafts in the Round Window. W. Hughson, Abington, Pa.—p. 533.
- Id.: (d) Surgery of Nasopharynx in Treatment of Chronic Progressive Deafness. H. Walker, Boston.—p. 552.
- Tuning Fork Tests Reported in Terms of Decibels. R. J. Hunter, Philadelphia.—p. 560.
- Use of Threshold and Louder Sounds in Clinical Diagnosis and Prescribing of Hearing Aids: New Methods for Accurately Determining Threshold for Bone Conduction and for Measuring Timulus and Its Effects on Obstructive and Neural Deafness. E. P. Fowler, New York.—p. 572.
- Xanthomatosis (Schüller-Christian's Disease): Report of Case with Radiosensitive Pathology in the Mastoid. J. J. Shea, Memphis, Tenn.—p. 589.
- Report on Result of Submitting Human Subjects to Rotation. E. R. Arellano, Havana, Cuba.—p. 599.
- The Endolymph. L. M. Polvogt, Baltimore.—p. 605.

Maine Medical Journal, Portland

29: 181-202 (Sept.) 1938

- Acute Respiratory Infections: The Upper Respiratory Tract. F. T. Hill and E. R. Jorgens, Waterville.—p. 181.
- Acute Infection in the Lower Respiratory Tract. D. S. King, Boston.—p. 189.
- Ocular Headaches: Some of Their Common Causes. L. H. Berrie, Houlton.—p. 195.

Michigan State Medical Society Journal, Lansing

37: 765-860 (Sept.) 1938

- The Diagnosis of the Right Lower Quadrant. F. Christopher, Evanston, Ill.—p. 783.
- Plastic Surgery in Relation to Motor Accidents. W. A. Lange, Detroit.—p. 787.
- Fracture of Neck of Femur. F. C. Kidner, Detroit.—p. 792.
- Primary Carcinoma of Jejunum. C. D. Brooks, W. R. Clinton and L. B. Ashley, Detroit.—p. 795.
- *Use of Dried Bile as Therapeutic Agent. J. M. Winfield, Detroit.—p. 798.
- Convulsions Occurring During Nitrous Oxide-Oxygen Anesthesia: Report of Case. C. Gittlin, Detroit.—p. 802.

Dried Bile in Gastrointestinal Disorders.—Winfield used dried bile (obtained by drying pig bile in high vacuum) in twenty-seven cases in which there was no loss of bile through drainage but in which there were symptoms which might have been attributable to a deficiency in the quantity or quality of bile in the intestinal tract. The chief symptom for which the dried bile was given was loss of appetite. Best results were obtained in those cases in which there was definite evidence of biliary disease. When the feeding of bile proved efficacious, the increase in appetite was evident usually within a few hours. In an occasional instance, however, anorexia increased even though the underlying factor, a definite biliary disorder, was corrected. Also the associated symptoms of belching, distention and constipation were materially affected in the majority of cases. Dried bile had a slightly laxative effect. The

preparation of dried bile used was soluble. The use of the dried bile forms a simple means of supplying additional bile so necessary for the absorption of vitamin K. The dosages used have been purely empiric. From two to three capsules were given three or four times a day. Each capsule contains 0.35 Gm. of dried bile. One gram of dried is the equivalent of approximately 9 Gm. of gallbladder bile. Since this is real hunger bile and hence quite concentrated, 1 Gm. is equal to at least 90 cc. of liver bile, according to the figures of Rous and McMaster regarding the concentrating activity of the gallbladder.

Missouri State Medical Assn. Journal, St. Louis

35: 343-384 (Sept.) 1938

- Medical Participation in a Public Health Program. T. R. Meyer, Clayton.—p. 343.
Hernia Reduced en Masse. A. D. Vail, Springfield.—p. 348.
Nonoperative Treatment of Incipient Cataract. G. H. Poos, St. Louis.—p. 350.
Rare Case of Typho-Ascariasis. O. Krueger, Kansas City.—p. 351.
Treatment of Syphilitic Psychoses with Tryparsamide and Therapeutic Fever. P. V. Dreyer, Huntsville.—p. 353.
Aseptic Uretero-Intestinal Anastomosis: Experimental Study. E. J. Jordan, St. Louis.—p. 356.
Sodium Desoxycholate Citrate and Selenite Mediums in Typhoid Fever Tests. Edna L. Smith, Jefferson City.—p. 361.
Self Medication: Report of Case. K. E. Pletcher, Eldon.—p. 365.

New England Journal of Medicine, Boston

219: 367-410 (Sept. 15) 1938

- *New Surgical Technic for Treatment of Postphlebotic Varicose Ulcers of the Lower Leg: Preliminary Report. R. R. Linton, Boston.—p. 367.
Osteoporosis in Hyperthyroidism: Reports of Two Cases with Compression Fractures of the Vertebrae. E. C. Bartels and G. E. Haggart, Boston.—p. 373.
Rocky Mountain Spotted Fever in Massachusetts: Report of Case. L. S. Pilcher, Newton Center, Mass.—p. 378.
Ingestion of Iodine as a Method of Attempted Suicide. M. Moore, Boston.—p. 383.
Ménière's Syndrome: Differential Diagnosis and Treatment: Case Report. R. J. Clark, Winchester, Mass.—p. 388.

Surgical Technic for Postphlebotic Varicose Ulcers.

—Linton recommends the following method of handling postphlebotic varicose ulcers. Cultures are taken before any dressings are applied. These usually show a mixed growth of bacteria; sometimes hemolytic streptococci are present, but most commonly staphylococci. The patient is placed in bed. A blood test is done to rule out syphilis. The leg with the ulcer is elevated on a pillow to the level of the heart or a little above it. Warm 2 per cent boric acid or saline solution compresses are applied to the ulcerated area every two hours. If hemolytic streptococci are present, compresses of surgical solution of chlorinated soda are most efficacious. Under this regimen the condition of the leg and of the ulcer improves rapidly. Unless streptococci have been discovered, the ulcer is usually in a satisfactory condition for cutaneous grafting at the end of a week. The graft requires from ten days to two weeks for a satisfactory take. At the end of this time the patient prepares himself for getting out of bed by doing postural leg exercises for three or four days. These exercises are a modification of those described by Buerger and Allen in that the period of elevation is longer than the period of dependency. When the patient is up he must wear a supporting elastic bandage. One or two days before he is discharged the long saphenous vein of the affected limb is ligated in the groin. Although this vessel may not appear to be varicose it is rare not to find it incompetent in the postphlebotic leg. Sometimes one of the communicating veins between the long saphenous vein and the deep veins in the thigh is incompetent. If such is the case this vessel should be ligated at the same time. If the short saphenous vein is involved it is ligated in the popliteal space. When the patient is discharged home an elastic adhesive bandage is applied directly to the skin from the toes to just below the knee. This is changed every two or three weeks. At the end of six weeks the patient returns to the hospital for ligation of the communicating veins. In the thirty-seven cases treated in this manner the wounds have healed by primary intention. The skin of the lower part of the leg should be carefully cleansed preoperatively with soap and water. If there is scaling or itch-

ing, a fungicide is applied twice a day until it is in a satisfactory condition for operating. The location of the ulceration guides one in deciding which group or groups of communicating veins should be ligated. If the ulcer lies on the inner aspect of the lower part of the leg the medial group of communicating veins and the popliteal communicating vein are ligated. If it lies on the anterior surface of the leg it is usually necessary to ligate the anterior group also. When the ulcer is on the posterior or posterolateral surface the lateral group and the popliteal communicating veins are ligated, and in addition the short saphenous vein is ligated in the popliteal space. In a few cases it may be necessary to ligate all the communicating veins. Normal veins are not ligated, so that actually a number of the vessels are preserved. If there is any question as to whether or not they are incompetent it is best to ligate them. The operation is done under spinal anesthesia. Silk is used as the suturing material. After the operation a posterior plaster shell is applied from the toes to just below the knee for immobilization so as to aid healing of the wound. The dressing is done first on the tenth day, when half the stitches are removed. The remainder are taken out from two to four days later, depending on the condition of the wound. If it is well healed, postural exercises of the leg are again instituted before the patient is allowed out of bed. The patient is discharged on the sixteenth to the eighteenth day if the wound is well healed and only one group of veins has been ligated. An elastic adhesive bandage is applied before discharge. This is worn for from two to three weeks. Thereafter a bender bandage or an elastic stocking is worn for a period of from three to six months. This is to control edematous formation. In some cases it is necessary to obliterate the superficial veins with injections of a sclerosing solution; in others this may not be required, as the varicose veins shrink to normal size after their communications with the deep veins have been severed. After several months some patients are able to discard supporting bandages, while others continue to wear them, either because of persistent edema or because of habit.

New Jersey Medical Society Journal, Trenton

35: 463-520 (Aug.) 1938

- Medical Management of Gastric Carcinoma. S. W. Johnsen, Passaic.—p. 467.
Reticulo-Endothelial System. M. Openchowski, Newark.—p. 468.
Vaccines in the Treatment of Disease. J. A. Kolmer, Philadelphia.—p. 472.
Serums in the Prophylaxis and Treatment of Disease. J. A. Kolmer, Philadelphia.—p. 478.
The True and False in Cardiac Diagnosis. C. Eggleston, New York.—p. 484.
Some Medical Ostracca. F. H. Church, Salem.—p. 489.
Vertigo of Ménière's Syndrome. T. S. P. Fitch, Plainfield.—p. 491.
Heart Disease in Pregnancy: Maternal Welfare Article Number Twenty-Eight. J. B. Gulick, East Orange.—p. 493.

35: 521-584 (Sept.) 1938

- Rheumatic Heart Disease in Children. J. G. Kaufman, Newark.—p. 525.
Coronary Vascular Disease. H. Halprin, Caldwell.—p. 531.
Tests for Drunkenness in Relation to Motor Accidents. G. Carter, London, England.—p. 537.
Discussion of Some of the Great Advances in Gastro-Enterology. H. M. Eberhard, Philadelphia.—p. 541.
X-Ray Diagnosis of Gastric Cancer. A. J. Delario, Paterson.—p. 548.
*Ozone in Oil: Preliminary Study of Its Therapeutic Value. L. F. Bender, Philadelphia, and K. Blanchard, East Orange.—p. 551.
Maternal Mortality Statistics 1937: Maternal Welfare Article Number Twenty-Nine. A. W. Bingham, East Orange.—p. 553.

Ozone in Oil.—During the past few months Bender and Blanchard used an ozonide of olive oil as a routine measure in more than 200 cases of acute coryza by instilling 5 or 10 drops in each nostril several times a day by means of an ordinary medicine dropper. In all cases the children were freed from mucous plugs, the nasal airway was cleared and respiratory distress was relieved. In the case of nurslings the routine use of a nasal suction pump about fifteen minutes after the instillation of a few drops has been of decided benefit. This prevents any interruption in the infant's ability to obtain air during the nursing period. Under such conditions the infant does not gulp its food and suffer from excessive air in the stomach. Several cases of impetigo have responded to the ozonide, with and without ultraviolet rays. Two cases of chronic fungoid

infection of the feet cleared up within three weeks. In several cases of eczema the cutaneous condition was greatly improved after consistent use of the ozonide of olive oil in conjunction with a regulated diet.

New Orleans Medical and Surgical Journal

91: 57-110 (Aug.) 1938

- The Family Doctor. C. C. de Gravelles, New Iberia, La.—p. 57.
Genito-Urinary Aspect of Syphilis. J. G. Menville, New Orleans.—p. 58.
Medical Aspects of Syphilis. E. Hull, New Orleans.—p. 60.
Cutaneous Syphilis. J. K. Howles, New Orleans.—p. 62.
Public Health Aspects of Syphilis. J. A. Trautman, New Orleans.—p. 71.
Presacral Sympathectomy. C. G. Collins, New Orleans.—p. 75.
Recent Advances in the Treatment of Pneumonia. C. L. Eshleman, New Orleans.—p. 77.
Conservative Obstetrics and Lowered Morbidity. W. F. Guerriero and C. P. Gray Jr., Monroe, La.—p. 82.
Immunotransfusion in Otolaryngology. M. G. Lynch, New Orleans.—p. 89.

Oklahoma State Medical Assn. Journal, McAlester

31: 261-294 (Aug.) 1938

- Acute Coronary Occlusion. W. S. Middleton, Madison, Wis.—p. 261.
Reconstruction Operation for Old Ununited Fracture of the Femoral Neck. P. C. Colonna, Oklahoma City.—p. 266.
Carcinoma of the Prostate. H. S. Brown, Tulsa.—p. 269.
Treatment of Infections of the Prostate. B. A. Hayes, Oklahoma City.—p. 270.
Acute Nephritis and Nephrosis. E. R. Mnsick, Oklahoma City.—p. 274.
Use of Caustery and Escharotics in the Nose. O. A. Watson, Oklahoma City.—p. 277.

Public Health Reports, Washington, D. C.

53: 1593-1634 (Sept. 9) 1938

- Percentage of Illnesses Treated Surgically Among 9,000 Families, Based on Nation-Wide Periodic Canvasses, 1928-1931. S. D. Collins.—p. 1593.
Two New Species of Ticks (Ixodes) from California (Acariua: Ixodidae). R. A. Cooley and G. M. Kohls.—p. 1616.

Rocky Mountain Medical Journal, Denver

35: 665-744 (Sept.) 1938

- Differentiation of Rash-Producing Epidemic Diseases. R. H. Verploeg, Denver.—p. 687.
Treatment of Pelvic Infections. W. P. McCrossin Jr., Colorado Springs, Colo.—p. 689.
Influence of Early Diagnosis on Surgical Treatment of Tumors of the Brain. W. M. Craig, Rochester, Minn.—p. 693.
Congenital Defects of the Nose, Lip and Palate: Practical Problems in Their Surgical Correction. A. C. Callister, Salt Lake City.—p. 698.
Tuberculosis Control. A. R. Masten, Denver.—p. 702.
Epistaxis: Etiology and Treatment. J. P. Rigg, Grand Junction, Colo.—p. 705.
Drugs and Narcotics. Sister Rose Paul, Denver.—p. 711.

Early Diagnosis in Cerebral Tumors.—Craig states that tumors of the brain diagnosed early are readily amenable to surgical treatment. This applies to the benign encapsulated tumors and the infiltrating malignant gliomas. However, in the early development of tumors of the brain the symptoms are sometimes so vague and uncertain that a definite diagnosis is impossible. In this event a patient can be given sedatives and kept under observation until more definite symptoms have developed or pneumo-encephalography or ventriculography can be carried out. Encephalography should never be undertaken in the presence of increased intracranial pressure, as evidenced by choked disks or papilledema. In the presence of increased intracranial pressure, ventriculography is the procedure of choice. A normal distribution of air in the subarachnoid space, in and around the convolutions of the cortex and within the ventricles rules out the possibility of intracranial tumor. Since the glioma group of tumors has been studied it has been realized that there are certain infiltrating tumors of the brain which, if completely removed with the surrounding tissue, will not recur. These are the tumors which it is important to diagnose before they have invaded too much of the cerebral substance. The more malignant types of tumors tend to recur even if completely removed. The use of high voltage roentgen therapy and radium in the treatment of the more malignant types of cerebral tumors has proved of value in a certain number of cases. The more radiosensitive types of tumor respond by an alleviation of the acute symptoms. Roentgenotherapy should augment surgery and should not be used as a primary method of treatment.

Virginia Medical Monthly, Richmond

65: 515-582 (Sept.) 1938

- The Lure of Medicine. H. A. Christian, Boston.—p. 515.
Of Sin and Punishment. J. K. Hall, Richmond.—p. 518.
Treatment of Burns. T. K. McKee, Saltville.—p. 522.
Biopsy of Cervix Uteri. W. H. Parker, University.—p. 523.
Injection of Internal Hemorrhoids. E. H. Terrell, Richmond.—p. 527.
Fractures of the Femur. M. H. Todd, Norfolk.—p. 527.
Prognostic Significance of QRS Changes in Acute Coronary Thrombosis. N. Bloom and Grace Cason, Richmond.—p. 530.
Lymphopathia Venerea (Lymphogranuloma Inguinale). L. W. Holladay, High Point, N. C.—p. 536.
The Surgical Emergency. H. W. Kinderman, Hampton.—p. 538.
Sinusitis, Office and Home Care. T. A. Poole, Washington, D. C.—p. 543.
Complex Consciousness in Religious Delusions: Case Report. L. L. Hallay, McClure.—p. 544.

Western J. Surg., Obst. & Gynecology, Portland, Ore.

46: 451-512 (Sept.) 1938

- Relation of Estrogenic and Gonadotropic Hormones to Climacteric Symptoms. Kathleen M. Murphy and C. F. Fluhmann, San Francisco.—p. 451.
*False Positive Wassermanns in Cerebrospinal Fluid. A. J. McLean, Portland, Ore., and I. C. Munger Jr., Vancouver, Wash.—p. 455.
Renal Changes Following Toxemias of Late Pregnancy. E. W. Page, Berkeley, Calif., and A. J. Cox, San Francisco.—p. 463.
Uterine Retrodisplacements, Retrograde Menstruation and Endometriosis. R. E. Watkins, Portland, Ore.—p. 480.
Endothelial Myeloma (Ewing's Sarcoma) with Metastases to the Vagina. A. Mathieu and P. H. Moore, Portland, Ore.—p. 495.
The Psychologic Abdomen: Its Surgical Importance: Division II. B. L. Diamond, San Francisco.—p. 498.

Falsely Positive Wassermann Reactions of Cerebrospinal Fluid.—McLean and Munger's interest in the circumstances of falsely positive reactions was aroused almost a decade ago by a case of craniopharyngioma in which, on the basis of a single determination of an indisputably positive Wassermann reaction of the spinal fluid (with negative reaction of the blood), prolonged arsphenamine treatment had been given elsewhere, despite progressive disabling and localizing intracranial signs. The Wassermann reaction of the spinal fluid and blood was negative when successful operation was done on the tumor. Because fluid from the craniopharyngioma usually contains abundant macroscopically visible cholesterol crystals, the assumption was currently made that such extravasated fluid might be the cause of the falsely positive Wassermann reaction. Further cases have since been sought and ten are reported (encephalomalacic atrophy, trauma, cerebrospinal rhinorrhea, electrical burn and neuritis). In most of these the common factor appears to be destruction or degradation of neuroprotein and neuropiloid in areas in which cerebrospinal fluid stasis is occurring—the teleologic function of the latter in these circumstances merely allows concentration of a reagent otherwise minimally present. The three most likely possibilities as to the nature of this unknown reagent may be as follows: 1. A reagin globulin truly analogous to syphilitic reagin may be elaborated directly during the degradation of neuroprotein. 2. Although the role of phanerated cholesterol appears innocent from the authors' experiments, other degradation neuropiloids (abnormal split products) present in such cerebrospinal fluid may combine with test antigen so as to sensitize the latter far beyond its usual titer and thus give rise to falsely positive reactions. 3. The mere presence of increased nonspecific protein produced during the degradation may, as in serum, offer such physicochemical inhibition of the usual measured dose of added complement for spinal fluid in routine tests that a falsely positive reaction would result. The minimum of laboratory work on any sample of spinal fluid should include cell count, differential count, and globulin, total protein, Kolmer and Lange tests. If the diagnosis indicated by laboratory tests is not in accord with the clinical observations, more fluid should be obtained and the tests should be repeated by two laboratories; the Wassermann-Kolmer test should then be done on spinal fluid with and without preliminary inactivation and the result should be checked by flocculation concentration tests. If the laboratory results still disagree with the clinical facts, the tests should be repeated in three or four weeks; if the reaction is still positive, specific therapy should be tried, though not before this.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Journal of Dermatology and Syphilis, London
50: 399-486 (Aug.-Sept.) 1938

- Recent Advances in Leprosy and Methods Adopted for Dealing with the Problem in France. C. Flaudin.—p. 399.
- *Question of Etiology of Pemphigus Vulgaris and Dermatitis Herpetiformis (Dühring's Disease): Clinical Experimental Study. A. Dostrovsky, I. Gurevitch and H. Ungar.—p. 412.
- New Technic for Epilation of the Scalp: To Provide More Even Distribution of Dose Than That Obtainable in Adamson-Kienbock Technic. E. H. Molesworth and H. L. Brose.—p. 435.
- Four Area Method in X-Ray Epilation of Scalp. S. C. Shanks.—p. 440.
- Match and Match-Box Dermatitis. R. Klaber.—p. 451.

Etiology of Pemphigus and Dermatitis Herpetiformis.

—Dostrovsky and his co-workers have carried out experiments since 1936 with the transmission of material from patients with pemphigus vulgaris and Dühring's disease. They used the contents of the vesicles, extract of the vesicular wall and blood serum of the patients. The injections were made into the cisterna, the brain and, to a smaller extent, intravenously into rabbits. There were no cutaneous manifestations on the rabbits, but disorders of the central nervous system occurred. This reaction is known to occur in other diseases which are caused by a filtrable virus; e. g., Hodgkin's disease and herpes zoster. There was a marked difference in the clinical picture of spontaneous encephalitis and that appearing in the rabbit during the experiments. The control experiments and the negative cases prove to the authors that spontaneous encephalitis is not encountered frequently. The most suitable material in the study was the vesicular fluid. The percentage of positive results achieved with this material was considerable. It was not dependent on whether it was sterile from the beginning or had to be filtered because of contamination. Cerebrospinal fluid also produced positive results. Experiments with blood serum were all negative except one. The best method of injecting the material to obtain positive results was into the cisterna. This fact impairs the value of the experiments to a certain extent, since it should be assumed that the virus injected under the dura of the experimental animal should bring about the same number of affected rabbits. It is possible that for intravenous injection more material is needed; i. e., a more massive infection. The authors succeeded in bringing about the clinical picture of encephalomyelomeningitis in 43 per cent of the rabbits. The condition has been verified by histologic examination in about 50 per cent of the cases. These facts lead them to the conclusion that, probably, there is some filtrable virus which produces pemphigus vulgaris and Dühring's disease belonging to the group of the neurotropic viruses and that the two diseases belong to the same group. Passage experiments furnished further proof for this hypothesis, although these experiments showed positive results in only three instances and in only the first passage. The possibility that the virus is an accompanying and not the true cause of pemphigus vulgaris and Dühring's disease should not be overlooked.

British Medical Journal, London

2: 387-436 (Aug. 20) 1938

- Rheumatoid Arthritis. W. Edgecombe.—p. 387.
- Orthopedics in Rheumatoid Arthritis. N. Capener.—p. 391.
- Effect of Spontaneous Jaundice on Rheumatoid (Atrophic) Arthritis: Attempts to Reproduce the Phenomenon. P. S. Hench.—p. 394.
- *Sulfamidochrysoidine, Sulfanilamide and Benzylsulfanilamide in Treatment of Erysipelas: Controlled Series of 242 Cases. W. R. Snodgrass, T. Anderson and J. L. Rennie.—p. 399.
- Late Results of Surgical Treatment in Perforated Peptic Ulcer. J. V. Cable.—p. 403.

Sulfanilamide Compounds and Erysipelas.—Snodgrass and his collaborators compared the therapeutic value in 242 cases of erysipelas of sulfamidochrysoidine (original prontosil), *p*-aminobenzenesulfonamide (sulfanilamide) and *p*-benzylaminobenzenesulfonamide (proseptasine). The patients were more than 5 years of age whose condition was diagnosed as erysipelas after admission to Ruchill Hospital. The 242 patients were divided into eight groups of thirty (fifteen male and fifteen female patients in each group) and each group received respectively at intervals of four hours 1 or 2 Gm. of prosepta-

sine, 1 or 2 Gm. of sulfanilamide, 1 or 2 Gm. of the prontosil or 0.5 or 0.75 Gm. of sulfanilamide. There were five deaths. Of fifty-eight patients receiving the prontosil 86.2 per cent had no further spread of the lesion after twenty-four hours; of the 120 patients receiving sulfanilamide the equivalent percentage was 88.3, while of the fifty-eight who received proseptasine the percentage was only 68.9. With regard to the various subgroups receiving sulfanilamide little can be said: there is a slightly better outcome during the first day for patients receiving the larger doses but the difference is small and insignificant. There is no significant difference between the various results. After forty-eight hours, pyrexia had ceased in 77.6 per cent of the patients receiving the prontosil, in 72.1 per cent of those receiving sulfanilamide and in 74.1 per cent of those receiving proseptasine. Of the fifty-eight patients receiving the prontosil the percentage having no toxemia after the third day was 65.6; the equivalent percentage was 59 for the 122 receiving sulfanilamide and 29.3 for the fifty-eight patients receiving proseptasine. These percentages reflect unfavorably on the action of proseptasine. No recurrence took place in any case during the period of stay in the hospital, nor has any patient been readmitted with a recurrence one month after the closing of the records. The incidence of complications was 13.8 per cent in those patients receiving the prontosil, 6.6 in those receiving sulfanilamide and 13.8 in those treated with proseptasine.

2: 437-480 (Aug. 27) 1938

- Toxic and Infective Jaundice. C. E. Lakin.—p. 437.
- Methods of Testing for Color Vision and Theoretic Deductions from Observations on Color Vision. H. E. Roaf.—p. 440.
- Some Cardiology Fallacies. J. W. Linnell and W. A. R. Thomson.—p. 442.
- *"Restropic" Activity of Blood. C. Wetzler-Ligeti and B. P. Wiesner.—p. 444.
- Treatment of Carcinoma in Pharynx and Larynx by Irradiation. C. Hamblen-Thomas.—p. 447.
- *Helium in Anesthesia. W. S. Sykes and R. C. Lawrence.—p. 448.
- Cardiazol Therapy in Stupor. J. S. Harris and C. R. Birnie.—p. 449.

"Restropic" Activity of Blood.—Wetzler-Ligeti and Wiesner find that the blood of rabbits, horses and healthy human subjects contains a factor that stimulates the activity of the reticulo-endothelial system (positive restropic factor). Positive restropic activity seems to persist in disease, except in malignant disease, when, as a rule, the normal activity is reversed and a negative restropic factor is found. The data show that disease in general, with the exception of malignant disease, does not fundamentally alter the restropic activity of the blood. As a rule a positive factor is present even in severe nonmalignant conditions. The concentration of restropin may be higher in some diseases than in health, but confirmation is required. Both in normal subjects and in various clinical conditions the concentration of positive restropin may fall so low that there may be no effect on the reticulo-endothelial system of the test animal. The origin of negative restropin is more obscure than that of the positive factor. In experiments with pituitary extracts negative activity was found to be associated with the thyrotropic factors; in the present experiments no obvious thyrotropic activity was noted to attach to the negative extracts. Moreover, these extracts were toxic in many instances—a property not observed in corresponding doses of thyrotropic extracts. The biologic significance of the observations under discussion is open to several purely provisional interpretations. It could be considered that the reticulo-endothelial system is involved in the maintenance of immunity and resistance; the presence of positive restropin possibly reflects or conditions the active state of the system. Conversely, the development of negative restropic activity in the blood might tentatively be regarded as a manifestation of a severe disturbance of the function of the reticulo-endothelial system. The fact that negative restropic activity has been demonstrated up to the present time only in cases of malignant disease is possibly significant, for it has long been assumed that the systemic changes that develop in malignant disease extend to the reticulo-endothelial system.

Helium in Anesthesia.—Since no patients with respiratory difficulties were available, Sykes and Lawrence carried out experiments on themselves, using artificial obstructions. The

found that an artificial atmosphere of helium and oxygen is theoretically and practically about twice as easy to breathe as ordinary air, and the mixture should be of great value in cases of respiratory obstruction or in cases in which it is essential to economize muscular effort. When obstruction is present its value is immediately apparent and can be measured by simple timing experiments. Even if there is no obstruction, in which case it has no visible effect, it might still be of value in reducing the amount of work done by the patient and, because of its low solubility, in preventing postoperative collapse of the lung.

East African Medical Journal, Nairobi

15: 129-164 (Aug.) 1938

- Treatment of Pulmonary Tuberculosis by Direct Injection of Lungs. H. N. Davies.—p. 135.
Strangulation of Spleen with Acute Intestinal Obstruction: Case. T. F. Anderson.—p. 141.
Night Blindness and Vitamin A in African School Boys. A. McKenzie.—p. 143.
Epithelioma in an Albino Native: Report of Case. M. Roberts.—p. 148.

Indian Journal of Medical Research, Calcutta

26: 1-326 (July) 1938. Partial Index

- Detection of Malnutrition by Measurements of Arm, Chest and Hip. W. R. Aykroyd, K. B. Madhava and K. Rajagopal.—p. 55.
Study of Myelin Degeneration in Polarized Light. M. V. Radhakrishnan Rao.—p. 103.
Variations in Iron Content of Foodstuffs and the Problem of Iron Requirements. S. Ranganathan.—p. 119.
Diet and Physique Survey in Assam, Rural Bengal and Calcutta. H. E. C. Wilson and D. D. Mitra.—p. 131.
Pyrophosphate in Determination of Vitamin C Content of Plant and Animal Tissues. K. V. Giri and N. S. Doctor.—p. 165.
*Vitamin C and Peptic Ulcer. M. Narasimha Rao.—p. 171.
Observations on Basal Metabolism of Healthy Subjects Under Varying Conditions of Temperature and Humidity. B. Ahmad, R. B. Lal and N. C. Roy.—p. 205.
Investigations into Epidemiology of Epidemic Dropsy: Part VI. Allylthiocyanate as an Etiologic Factor in Epidemic Dropsy. R. B. Lal, B. Ahmad and S. C. Roy.—p. 213.
*Virus of Sandfly Fever in Culture and Certain of Its Properties. H. E. Shortt, C. G. Pandit and R. Sanjiva Rao.—p. 229.
Some Biochemical Characteristics of Snake Venom. A. C. Roy and R. N. Chopra.—p. 241.
Use of Nonspecific Substances in Production of Tetanus and Diphtheria Antitoxin. D. C. Lahiri.—p. 311.
Immunization of Horses for Production of High-Titer Tetanus Antitoxin. Part II. N. N. Ray and G. C. Das.—p. 317.

Vitamin C and Peptic Ulcer.—Narasimha Rao estimated the vitamin C content of the blood of fifteen patients with peptic ulcer. A variation of from 0.4054 to 1.92 mg., with an average of 0.8971 mg., was observed. These values are nearly identical with values in healthy control subjects. Therefore he concludes that there is no gross vitamin C deficiency in patients suffering from gastric or duodenal ulcers.

Virus of Sandfly Fever.—Shortt and his associates cultivated the virus of sandfly fever by the chorio-allantoic membrane technique and in tissue culture. The cultures were carried through numerous passages. The serums of patients who had recovered from sandfly fever possessed the power of neutralizing the cultured virus. The animal inoculation experiments of the cultured virus by the intracerebral, intranasal, intraperitoneal and subcutaneous routes gave inconclusive results.

Journal of Physiology, London

93: 173-304 (Aug. 15) 1938

- Mechanism of Inhibition and Excitation of Crayfish Muscle. G. Marmont and C. A. G. Wiersma.—p. 173.
Changes in Muscle Contraction Curves Produced by Drugs of Eserine and Curarine Groups. Grace Briscoe.—p. 194.
Degenerative Changes in Axis Cylinders of Dental Nerves Due to Diets Deficient in Vitamin A and Carotene. J. D. King, W. Lewinsky and D. Stewart.—p. 206.
Action of Eserine-like and Curare-like Substances on Responses of Frog's Nerve-Muscle Preparations to Repetitive Stimulation. S. L. Cowan.—p. 215.
Dependence of Activity of "Apneustic Center" on Carbon Dioxide of Arterial Blood. G. Stella.—p. 263.
Micro Blood Volume Method Using Blue Dye and Photocell. J. A. Kennedy and G. A. Millikan.—p. 276.
Neuromuscular Conduction in the Fowl. G. L. Brown and A. M. Harvey.—p. 285.
Plethysmographic Method for Measuring Systolic Blood Pressure in the Intact Rat. F. B. Byrom and C. Wilson.—p. 301.

Lancet, London

2: 409-466 (Aug. 20) 1938

- Rhythm in Epilepsy. G. M. Griffiths and J. T. Fox.—p. 409.
Tropical Macrocytic Anemia: Its Relation to Pernicious Anemia. Lucy Wills and Barbara D. F. Evans.—p. 416.
Meningo-Encephalitis and Orchitis as the Only Symptoms of Mumps. W. Harris and H. Bethell.—p. 422.
Some Biologic Properties of Diethylstilbestrol. S. J. Folley and Helen M. S. Watson.—p. 423.
Chronic Meningococcal Septicemia Treated with 2-(p-Aminobenzenesulfonamido) Pyridine. S. B. Dimson.—p. 424.
*Stomatitis of Vitamin B₂ Deficiency Treated with Nicotinic Acid. P. Manson-Bahr and O. N. Ransford.—p. 426.
Paralysis of External Pterygoid Muscle Arising from Injury to the Fifth Cranial Nerve. H. Gardiner.—p. 428.

Vitamin B₂ Stomatitis and Nicotinic Acid.—Manson-Bahr and Ransford draw attention to the benefit which may attend the administration of nicotinic acid in states which can be described as prepellagrous. An instance of sore tongue is cited. In temperate climates the cutaneous lesions of pellagra do not appear and deficiency of the pellagra-preventing factor shows itself by stomatitis, a characteristic desquamation of the tongue and chronic diarrhea. The case cited is that of a woman of 62 who had suffered from these symptoms for five years and recovered rapidly with 150 mg. of nicotinic acid daily for ten days and a full diet. The authors believe that many similar cases are encountered in general practice in England.

2: 549-602 (Sept. 3) 1938

- The Iron Deficiency Anemias. R. B. Scott.—p. 549.
Angle of Abduction of Hip After Subtrochanteric Osteotomy. H. J. Seddon.—p. 552.
Experimental Exchange Transfusion Using Purified Heparin. W. Thalheimer, D. Y. Solandt and C. H. Best.—p. 554.
*Use of Synthetic Desoxycorticosterone Acetate in Addison's Disease. S. L. Simpson.—p. 557.
Acute Ulcerative Stomatitis. E. W. Fish.—p. 558.
Hyperplastic Tuberculosis of the Cecum, with Special Reference to Radiologic Diagnosis. F. G. Wood and M. C. Wilkinson.—p. 560.
*Antibacterial Power of Blood of Patients Receiving 2-(p-Aminobenzenesulfonamido) Pyridine. A. Fleming.—p. 564.

Desoxycorticosterone Acetate in Addison's Disease.—Simpson found a synthetic product, desoxycorticosterone acetate, approximating in chemical formula to corticosterone, effective in two patients with Addison's disease. It has a therapeutic action in Addison's disease similar to that of extract of the suprarenal cortex (cortin). From the cases recorded it appears that 6 mg. of desoxycorticosterone acetate (1 cc. of oily solution) is equivalent to more than 5 but less than 20 cc. of cortin. The first patient, with severe suprarenal insufficiency, gave an equivocal response, but the second was undoubtedly benefited to a far greater degree than when receiving cortin. The injections were given intramuscularly and were not painful, although a transient localized stinging sensation sometimes resulted.

Blood After Sulfanilamide Compound.—If 2-(p-aminobenzenesulfonamido) pyridine acts by virtue of its bacteriostatic power then the blood of patients taking it should possess an increased power of restraining the growth of bacteria that are sensitive to its action. Fleming describes experiments showing that the action of the blood of patients taking the drug does not differ materially from the action (described in an abstract in THE JOURNAL Sept. 17, 1938, page 1140) of blood mixed with the chemical after withdrawal from the body. The blood specimens used in these experiments were taken from three patients who were being treated with the drug. The blood of the patients has a much increased antibacterial power against hemolytic streptococcus and pneumococcus. This increased antibacterial power resides in the serum. The efficiency of antibacterial power is not increased. A patient's serum which is the leukocytes is not increased. A patient's serum which is strongly inhibitory to streptococci is incapable of killing the cocci in two days. The patient's serum not only inhibits growth but also inhibits the production by Streptococcus pyogenes and pneumococcus of substances which alter the blood. The drug added to human blood or contained in the blood of patients taking the chemical does not prevent encapsulation of pneumococci. A more likely mode of action is simple inhibition of growth (and possibly of toxin production), and while the organism's growth is stopped and its vitality lowered some agent in the body damages the capsule, or perhaps some autolytic process occurs.

Archives des Maladies de l'Appareil Digestif, Paris
28: 673-792 (July) 1938

- Role of Fats in Glycogenesis and Utilization of Alimentary Proteins. F. Maignon.—p. 673.
Duodenal Triage with Aid of Pliant Rubber Tube Provided with Mandrin. C. S. Schlumberger.—p. 689.
*Pathogenic Importance of "Lambliia Intestinalis." L. de Friedrich.—p. 693.
Pharmacodynamic Research on Morphology of Cellular Secretions. G. Wallbach.—p. 722.

Pathogenic Importance of Lambliia Intestinalis.—De Friedrich has observed forty cases of infestation with *Lambliia intestinalis* since 1927. He lists in tables the ages of the patients, the duration of the lamblasis and the chief complaints of the patients. He shows that diarrhea is the most frequent symptom; that a large number of patients complain of pains in the biliary region and that others have various gastrointestinal disorders. He observed a grayish-yellow and swollen appearance of the face in some of the cases, but he does not consider this necessarily characteristic for lamblasis. The gastric acidity is normal in the majority of cases. Roentgenoscopy of stomach and intestine reveal normal conditions in the majority and cholecystography generally discloses that the gallbladder is well filled. After discussing the examination of the feces, particularly the search for lamblia, the author shows that examination by means of the duodenal tube is the best method for the detection of lamblasis. The question whether lamblasis always requires treatment he answers in the affirmative, because he is convinced that it is harmful for the organism. He admits that as yet no specific remedy is available for lamblasis. He lists the various therapeutic substances that have been recommended. He himself tried emetine, and the intravenous and intraduodenal administration of nearsphenamine, also methylene blue and acriflavine hydrochloride. He regards the intraduodenal administration of arsphenamine combined with duodenal lavage as the best treatment. To be sure, relapses are frequent; there are spontaneous remissions in connection with the maturation of the organisms. *Lambliia* may appear as a harmless parasite; nevertheless, it is never certain when the time will come when the lamblia will multiply and provoke disturbances, and so it is always advisable to institute treatment when lamblia are detected. Cholecystectomy is not indicated, because it does not cure, and there is no definite proof that lamblia are constantly in the gallbladder. The functional disorders are caused by their presence in the duodenum and by their multiplication. Moreover, the lamblia may cause other disorders and so it is necessary to examine the entire digestive tract in order not to overlook an ulcer, cholelithiasis and so on.

Bulletin de la Soc. de Gynéc. et d'Obst., Paris

27: 405-484 (June) 1938

- *Clinical and Physiologic Bases of Functional Uterine Hemorrhages Caused by Hormone Disturbances of Ovaries. C. Bclère.—p. 405.
Study of Speed of Sedimentation of Erythrocytes in Gynecology. E. Renwa.—p. 413.
Remarks on pt of Cervical Orifice. Palmer and Michon-Adjonbel.—p. 416.
Two Roentgenograms of Intracervical Cancer Discovered by Means of Lipiodol. P. Lejeune.—p. 420.
Fetal Heart Sounds in Pregnant Women: Phonocardiographic Method. C. Lian, V. Golblin and G. Minot.—p. 423.

Uterine Hemorrhages from Hormone Disturbances.—Bclère discusses the clinical and physiologic bases of functional uterine hemorrhages of ovarian origin which indicate not only the close relations between abnormal functional hemorrhages and normal menstrual hemorrhages but also the intimate connections between functional hemorrhage and the hormonal action of the ovary. Summarizing the clinical aspects of the uterine hemorrhages before and after the menopause, he states: 1. There is the spontaneous menopause, which leads to spontaneous cure of functional premenopausal hemorrhages after years of disturbances and hemorrhages. 2. In two thirds of the patients with premenopausal functional hemorrhages there exists a pathognomonic clinical syndrome, which has three characteristic aspects: (a) sudden irregularity of the normal menstrual periods, (b) complete disappearance of the normal menstrual hemorrhages, which are replaced by irregular menometrorrhagias, (c) phases of amenorrhea alternating with hemorrhagic phases. 3. In other cases (about 10 per cent), the clinical syndrome is

purely menorrhagic; the menses preserve their normal periodicity. 4. In another 10 per cent of the cases, the syndrome is entirely polymenorrhagic; that is, the rhythm of the menses is shortened. 5. There are two particular clinical conditions which are intermediate between the normal menopause and the premenopausal functional hemorrhages: (a) menopause in stages in which amenorrhagic phases alternate with phases of normal menstruation; (b) menopause with irregularity of the normal rhythm of the menses but with conservation of the normal duration and abundance. In giving his attention to the physiologic aspects he shows that the cause of these uterine hemorrhages is a hormonal disorder of the ovary and that their physiologic mechanism is the same as that of the normal menstrual flow. He points out that abnormal uterine hemorrhages as well as the normal menstrual flow can be made to disappear by the surgical removal of the ovaries, without the uterus being touched. Moreover, roentgen therapeutic suppression of the functional activity of the ovaries will accomplish the same. In some cases of functional hemorrhages an excess of estrogenic substance has been demonstrated in the blood and urine. Moreover, glandular hyperplasia has been produced after ovariectomy by means of the administration of large doses of estrogenic substance. He emphasizes that functional hemorrhages, like the normal menstrual flow, are provoked by the hormonal secretion of the ovary. Both are accompanied by modifications of the uterine mucosa and both are, by way of the ovary, partly dependent on the secretion of the anterior hypophysis. The author further reviews the results of the extirpation of the ovaries in animals and in women. Discussing the hormone therapy, he says that if there exists an excessive stimulation of the anterior lobe of the hypophysis in functional hemorrhages, the treatment should consist in checking the hypophysis. In order to check the hypophysis without stimulating the ovary, androgen is injected. Favorable effects have been reported with this treatment in some uterine hemorrhages of young girls, in premenopausal hemorrhages and in cases of fibroma.

Schweizerische medizinische Wochenschrift, Basel

68: 1025-1044 (Sept. 3) 1938. Partial Index

- Pathogenesis of Neurasthenia According to Theories of Janet. L. Schwartz.—p. 1025.
*Addition of Vitamin C to Histidine in Treatment of Gastroduodenal Ulcer. M. Demole and P. Guye.—p. 1028.
*Benzedrine in Treatment of Postencephalitic Parkinsonism. M. Dressler.—p. 1031.
When and Where Does Cyanosis Exist? K. Lenggenhager.—p. 1032.
New Aspects of Diagnosis of Gonorrhea of Female Urogenital Apparatus. M. Spitzer.—p. 1034.

Vitamin C and Histidine in Gastroduodenal Ulcer.—Demole and Guye point out that observations in recent years have raised the question whether a deficiency of vitamin C might be an etiologic factor in gastroduodenal ulcer. Clinical as well as experimental studies seem to lend support to this theory. The authors having obtained comparatively favorable results with histidine in the treatment of gastroduodenal ulcer, they decided to combine histidine and vitamin C. Since October 1936 they treated patients with gastroduodenal ulcer systematically with a histidine preparation to which ascorbic acid had been added. The preparation that they employed contained, in ampules of 5 cc., 0.209 Gm. of hydrochloride of histidine and 0.176 Gm. of ascorbic acid. Daily intramuscular injections was the mode of administration. The number of injections varied. The prescribed number for a series was twelve and only in especially refractory cases was the number increased to eighteen. The combination of histidine and ascorbic acid was employed in forty-eight cases, and although the authors regard a definite evaluation of this treatment as premature, they compare the results of the combination therapy with those produced by histidine alone. Of thirteen patients, who previously had been unsuccessfully treated with histidine, ten could be considered cured by the addition of ascorbic acid. The authors suggest that the presence of an adequate or excessive amount of ascorbic acid in the organism favors the cure of the ulcer, in that, after the ulcerous region is modified by the ascorbic acid, the histidine can exert its action more effectively. If, as they think, the ascorbic acid does not exert a direct, causal effect on the gastroduodenal ulcer, but rather favors cicatrization and intensifies the action of histidine, the question arises whether other vitamins

"Scarlet Fever Heart" and Anemia.—In this paper von Kiss and Malaguzzi-Valeri report their studies on a possible connection between anemia in scarlet fever and the syndrome of "scarlet fever heart." These investigations were made on thirteen children with scarlet fever. It was found that reductions in neither the erythrocyte count nor the hemoglobin played a part in the development of "scarlet fever heart."

Klinische Wochenschrift, Berlin

17: 1169-1208 (Aug. 20) 1938. Partial Index

Relations of Idiosyncrasy to Anatomic Structure of Epidermis. II. T. Schreus.—p. 1171.

*Treatment of Rickets with Concentrates of Vitamin D₂ and Vitamin D₃. G. Jacoby.—p. 1173.

Experimental Studies on Oral Insulin Therapy by Adding Organic Dye-stuffs. F. Lasch and E. Schönbrunner.—p. 1177.

Resorption of Orally Administered Tetra-Iodophenolphthalein. W. Lutz.—p. 1180.

First Changes of White Blood Picture in Persons Exposed to Lead Poisoning. A. H. Müller.—p. 1183.

Investigations on Possibility of Transmission of Tuberculosis by Children. A. Viethen.—p. 1186.

Carcinomas in Young Persons and Children. J. Körbler.—p. 1194.

Concentrates of Vitamins D₂ and D₃ in Rickets.—Jacoby treated twenty-three children with vitamin D₃ during the winter 1936-1937 and compared the results with those which were obtained in children who were treated with vitamin D₂. However, the comparison of the roentgenograms and of the chemical values of the blood did not corroborate the more favorable action of vitamin D₃, an assertion which had been made by Hartenstein and especially by Brockmann. When a vitamin D₂ concentrate became available, Jacoby hoped that vitamin D₃ would also become obtainable in a concentrate, because he thought that in view of the more rapid and intensive curative power of the concentrates a possible difference in the efficacy of vitamins D₂ and D₃ would be detected more quickly. The author made systematic studies on the chemistry of the blood and roentgenograms in twenty-four children who were treated with vitamin D₃ concentrate and in twenty-two children who were treated with vitamin D₂ concentrate. No noticeable differences could be detected in these two groups, in either the clinical, roentgenologic or hematochemical aspects. The vitamin D concentrates had an especially favorable effect on spasmophilia. There were twelve children with manifest and seven with latent spasmophilia. With the exception of two unusual cases, the convulsions never returned. The manifest type did not develop in any of the children with latent spasmophilia and spasmophilia did not develop in any of the other children with rickets. Children with severe rickets were given twice 15 mg. of the concentrate. A dose of 15 mg. of vitamin D₂ concentrate did not cure craniotabes.

Medizinische Klinik, Berlin

34: 1021-1052 (Aug. 5) 1938. Partial Index

Aspects of Painful Cardiovascular Phenomena. R. Schmidt.—p. 1021.

Clinical Aspects of Intoxications Caused by Inhalation of Gases. G. Budelmann.—p. 1029.

Familial Epidemic of Psittacosis. E. Woenckhaus.—p. 1032.

*Treatment of Lochiometra with Quinine Calcium. A. Richard.—p. 1036.

Treatment of Lochiometra.—Richard shows that in the treatment of lochiometra the main problem is to counteract the weakness of the uterine contractions to overcome the stasis of the lochia. Moreover, the development of a septic endometritis from the lochiometra must be prevented. The author says that both of these aims can be realized by the administration of a quinine calcium compound which in 10 cc. contains 0.6 Gm. of quinine gluconate and 1 Gm. of calcium gluconate. The ecbolic effect of the combination of quinine and calcium has been clinically demonstrated and the author recommends the intravenous administration of 10 cc. of the quinine calcium preparation in all cases of lochial stasis. If the stasis is due to spastic conditions of the internal uterine os, the author precedes the injection of quinine calcium by introducing suppositories containing the alkaloids of belladonna. The intravenous injection of the quinine calcium must be made slowly (five minutes for the 10 cc.) because rapid injection might cause collapse. If the temperature increases again, the injection can be repeated eventually by the intramuscular method. A third and fourth injection are

rarely necessary. The author has resorted to this treatment with quinine calcium so far in eighty cases of lochial stasis. He gives brief histories of ten cases and concludes that, by counteracting the febrile lochial stasis, the administration of quinine calcium is a valuable aid in preventing puerperal infections.

Münchener medizinische Wochenschrift, Munich

55: 1217-1256 (Aug. 12) 1938. Partial Index

Dietetic Treatment of Surgical Disorders. H. J. Lauber and R. R. Strack.—p. 1217.

Value of Digital Examination of Rectum in Gynecology. M. Köhler.—p. 1220.

Embolism in Diphtheritic Circulatory Disturbance. H. Zischinsky.—p. 1221.

*Trophic Changes of Skin in Chronic Pancreatitis. W. Grott.—p. 1224.

Nephritis with Fulminant Course. P. Heilmann and H. Eck.—p. 1225.

Insidious Sequels of Umbilical Infections in Nurslings. E. Calderón.—p. 1226.

Treatment of Diabetes Mellitus with Yeast. W. Beckert.—p. 1231.

Skin in Chronic Pancreatitis.—Grott maintains that chronic pancreatitis is comparatively frequent, but that it is not always recognized. Symptoms that make possible its diagnosis by means of the simple physical methods of examination available to the practitioner are the hyperesthesia of the pancreatic zone and the painful point at the body of the pancreas, which can be detected by the palpatory method, previously described by the author in the *Archiv für Verdauungskrankheiten* (58:181 [Oct.] 1935; abstr., THE JOURNAL, Dec. 21, 1935, p. 2117). In the present report the author directs attention to the presence of trophic changes of the skin in the pancreatic region; that is, in the upper left quadrant of the abdomen. To determine this trophic change the skin is laid into a fold and the thickness of the subcutaneous fat tissue is compared on the left and right sides, above and below the umbilicus, over the rectus muscle and outward from it. If the trophic change is present, the fold of skin is thinner in the region of the pancreas and the skin can be more readily lifted from its base than is the case in the other regions. Having observed this sign, the author watched for it and detected it in fifty-two patients. In twenty-one of these patients only a chronic pancreatitis existed and in thirty-one it was accompanied by diabetes mellitus; that is, the sign is characteristic for pancreatic diseases, particularly for chronic pancreatitis. Although this symptom alone does not permit the diagnosis of pancreatitis, together with other signs, it is a valuable diagnostic aid. If the trophic change is observed in patients with diabetes mellitus, it suggests a disease of the pancreas as the primary cause of the disease. A decrease or increase in the trophic change may run parallel with the pancreatic disorder; its persistence in spite of general improvement suggests that the pancreatic disturbance has not entirely subsided.

Khirurgiya, Moscow

1-168 (No. 8) 1937. Partial Index

*Complications Due to Application of Clamps After Resection of Stomach for Peptic Ulcer. L. V. Serebrenikov and V. P. Snezhkov.—p. 3.

Perforation of Duodenal Ulcer into Peritoneal Cavity. M. M. Levin.—p. 55.

*Alcoholization for Alleviation of Pain in Gastric Cancer and Gastric Ulcer. G. V. Pereiman.—p. 61.

Causative Factors of Death in Intestinal Obstruction. I. B. Oleskevich.—p. 80.

Obstruction of the Cecum. M. F. Camaev.—p. 88.

Appendicitis and Right Sided Perivisceritis. L. J. Posviatsky.—p. 91.

Complications After Resection of Stomach.—Serebrenikov and Snezhkov consider that the main cause of early and late complications after resection of the stomach and gastroenterostomy, such as gastric hemorrhage, separation of the sutures of the stump, subdiaphragmatic abscess, subperitoneal phlegmons and marginal ulcers, appears to be the method of using clamps. The authors carried out thirty-two experiments on ten dogs. Clamps were applied on the antral part of the stomach in fifteen experiments in the first series and on the jejunum in sixteen experiments of the second series. The Doyen and Linnartz types of clamps were employed. These were applied for from twenty-five to forty-five minutes, locked

on the third indentation of the lock. Sections of tissue were taken immediately after removal of the clamps and twenty minutes after the stomach wall appeared to be recovered. A study of the macroscopic and microscopic picture of the stomach and intestinal walls was carried out after the removal of the clamps. Altogether 124 pathologic preparations were examined. The changes found were as follows: severe traumatization of all layers of the stomach and intestinal walls, especially of the mucosa, which appeared completely crushed; a considerable amount of extravasation was observed at a considerable distance from the lesion; displacement of the various layers of the wall of the stomach with relation to each other, with formation of cavities filled with blood and thrombosis and necrosis of the vessels of the stomach and intestinal walls and of the vessels of the omentum and mesentery, was observed. The authors estimated that the extent of pressure exerted by the Doyen clamps equaled 9 Kg. for each centimeter of surface of the branches and that by the Linnartz clamps was 17 Kg. On the basis of their experimental data the authors recommend, in cases of resections for cancer of the stomach in which the employment of clamps is unavoidable, the use of the Spasokukotzky type, exerting less pressure, and in cases of ulcer an operative procedure in which no clamps are employed.

Alcoholization for Gastric Cancer and Gastric Ulcer.

—Perelman states that the method is based on the fact that alcoholization causes a break in the nervous tissue. From 15 to 20 cc. of an 80 per cent solution of alcohol was used for this purpose. In order to effect a break in the neurofibers of the sympathetic, passing through the stomach and alleviation of the pain in cases of inoperable cancer or gastric ulcer, injections should be made into the lesser omentum or, if the usual technic is to be employed, a splanchnic anesthesia is to be induced. The author reports twenty-two cases of alcoholization: in ten splanchnic anesthesia was carried out, in ten injections of alcohol were given in the lesser omentum and in two combined injections were given. The result of alcoholization was favorable, since it caused cessation of pain for from one and one-half to six and one-half months in cases of inoperable cancer. In cases of callous ulcer penetrating into the neighboring organs and in cases of pain in organs not innervated by the gastric nerve (liver), no effect is accomplished by this method. It may even cause an increase of pain, since injections of alcohol increase inflammatory adhesions.

Geneeskundig Tijdschr. v. Nederl.-Indië, Batavia

78: 1851-1912 (Aug. 2) 1938. Partial Index

Macrocytic Blood Pictures. L. Schalm.—p. 1851.

*Immunization Against Weil's Disease with Living Avirulent Leptospira. P. H. Van Thiel.—p. 1859.

Anthropologic Studies on Inhabitants of Central Celebes: I. Blood Groups. J. W. Tesch.—p. 1875.

Immunization Against Weil's Disease.—Van Thiel reviews some of the earlier experiments with the preparation of a vaccine for Weil's disease and then describes his own attempts at immunization by means of living avirulent cultures of leptospira. His experiments were made with a strain that was kept in culture for eight years without passage through animals. Its behavior in guinea pigs indicated that during the last years it was avirulent or practically avirulent for the animals. The author tried the subcutaneous injection of 2 cc. of the avirulent strain of leptospira on himself and as a result passed through a very mild; atypical attack of Weil's disease. He further describes the reactions of four other persons who volunteered to be injected with the avirulent strain. All of them passed through an atypical attack of Weil's disease; in two of them it was practically symptomless, in one the symptoms were mild, but in another the symptoms were so severe that the volunteer had to stay in bed. The author shows that the stronger reaction in the latter patient was caused neither by the injection of too large a dose nor by the accidental appearance of comparatively virulent leptospira but was probably the result of the person's disposition. This case proves that the injection of avirulent strains of leptospira is not entirely without risk and danger. The author says that if none of the persons had shown more severe reactions than

he himself or the one who had only mild symptoms, he might have recommended the more general application of this method of immunization. However, since the one case convinced him that the disposition of the person plays an important part and that leptospira which are avirulent for guinea pigs may cause reactions that are more severe than is permissible for immunization procedures, he intends to refrain from the further use of this method. Guinea pigs are apparently much less susceptible to Weil's disease than are human subjects and thus these investigations proved once more the erroneousness of the conclusion that observations on guinea pigs can be applied to human subjects.

Nordisk Medicinsk Tidskrift, Stockholm

16: 1271-1302 (Aug. 13) 1938

"Cotton Dust Disease." Occupational Disease Among Operatives Exposed to Cotton Dust. E. Trier.—p. 1271.

Idiosyncrasy to Quinine in Treatment of Varices. O. Arnell.—p. 1277.

Congenital Stenosis of Nasal Duct, Its Complications and Treatment. K. O. Granström.—p. 1280.

Easily Borne and Economical Method for Administration of Oxygen. B. Scherstén.—p. 1283.

*Death Due to Histamine: Case. P. Majjala.—p. 1287.

New Fixation Ocular for Determination of Field of Vision in Unilateral Central Scotoma. Å. Lundberg.—p. 1289.

Death from Histamine.—Majjala's patient, a man aged 32, with a history of gonorrhea, had had attacks of pain in the stomach region and slight dyspnea on exertion for a half year. The heart tones were clear except for a weak systolic murmur over the apex and the second intercostal space on the left edge of the sternum; the second aortic sound was slightly accentuated. Syphilitic aortitis was suspected. To investigate the nature of the patient's achylia a histamine test breakfast was given (0.8 mg. of histamine subcutaneously). Death occurred half an hour later. Necropsy showed syphilitic aortitis, the orifices of the coronary artery being almost completely obstructed by scar tissue. The aorta was not dilated. The histamine is believed to have caused circulatory disturbances, and the cause of death was acute cardiac insufficiency. The author cautions against the use of histamine in patients with aortic or suspected aortic disturbances.

Ugeskrift for Læger, Copenhagen

100: 871-896 (Aug. 4) 1938

*Failure of Tetanus Prophylaxis. J. Hertz.—p. 871.

Acute Porphyria: Two Cases in Siblings. R. Hammen.—p. 878.

Double Vagina and Double Uterus with Delivery: Three Cases. P. Freudenthal.—p. 883.

Limitis Plastica with Stenosing Intestinal Metastases. H. Gormsen.—p. 886.

Failure of Tetanus Prophylaxis.—Hertz reports three cases in which prophylactic injection of tetanus antitoxin was given and in which a well defined tetanus developed, with fatal outcome in two, in spite of energetic treatment. He says that the part played by the mixed infection which must have been present is uncertain. In one case there was extensive gangrene, and primary excision of the wound edges, done in the other cases, had not been performed. From the literature and his personal observations he concludes that, in lesions subject to infection with tetanus, prophylactic injection intramuscularly is called for as soon as possible, preferably immediately after the lesion, together with careful wound treatment with primary excision of the wound edges and removal of necrotic tissue. In case of constant suppuration in the suspected wounds the antitoxin injection should be repeated at suitable intervals of from about eight to ten days. Since every mechanically acting secondary trauma involves the danger of the occurrence of manifest tetanus, the antitoxin injection should be repeated before a surgical reintervention. The secondarily injected antitoxin is eliminated even more rapidly than that of the first injection and thus affords protection for a shorter time. If, in spite of the prophylactic measures, tetanus appears, amputation must not be delayed too long, as it eliminates the focus from which the bacilli send out their toxins. The only danger connected with the injection is that of anaphylactic shock, and anaphylactic reactions from prophylactic injections of tetanus antitoxin are exceedingly rare.

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ROENTGENOGRAPHIC STUDIES OF THE URINARY TRACT DURING AND AFTER PREGNANCY

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Urographic study of the upper urinary tract in pregnancy has been the subject of several recent contributions to the literature. Our present purpose is to review briefly the various salient features already stressed and add several of our own concepts, gained from a study of sixty consecutive unselected normal pregnancies. In limiting our study to intravenous or excretory urography, it was intended to investigate the physiology of the upper tract free of any mechanical intervention. Particular attention was placed on studies taken with the patient in the upright position, since it is our belief that renal mobility and nephroptosis is a vital factor in predisposing to complications.

Patients were taken as they presented themselves at the antepartum clinic of the Bayonne Dispensary. Each had been investigated from a medical and an obstetric standpoint and was apparently normal. Urinalysis in each instance was likewise free of pathologic conditions. The stage of pregnancy when first seen varied from one month to nine months.

In all patients a preliminary plate of the abdomen was taken prior to the injection of 20 cc. of diodrast. Radiographic exposures were then made in the supine position at five, thirty and sixty minute intervals, while an upright exposure was made at the end of fifteen minutes (figs. 1 and 2). Maximum excretion of the dye was most often noted at the end of thirty minutes, although the majority of the five minute exposures showed well delineated pelvis. Definition in most of the plates was somewhat obscured by the increased density and depth of penetration necessary. We feel that this is a vital factor in the apparent delay in excretion of the dye during pregnancy.

When possible, excretory urography was carried on at monthly intervals. In several instances five studies as outlined were obtained during the antepartum and postpartum investigation of the patient. The pregnant woman was found to tolerate the injection well, and no apparent ill effect was noted on the fetus in utero or the newborn, either from the drug or from the exposure to roentgen rays.

An interesting problem arises in connection with the use of a complex halogen and the roentgen ray during pregnancy. Does diodrast or a similar preparation reach the fetus through the placental circulation? Is there any danger of iodism in the fetus if such transmission does occur? May it be possible by refined radiographic technic to show the presence of dye in the urinary tract of the fetus during the final months of pregnancy? It is known that the fetal kidneys function during the last few months of pregnancy.

Further, what effect does the brief repeated exposure to the roentgen rays during the course of one or more excretory urograms have on the mother and fetus? In some instances, owing to the need for depth of penetration, an exposure time of four seconds was necessary. Scrutiny of the various contributions in the past has not considered this very vital problem.

Miller, Corscaden and Harrar,¹ after reviewing the literature on the effects of radiation on the human offspring, conclude that "it seems reasonable to advise that the use of radium and x-ray during pregnancy for treatment purposes be restricted to very clear and urgent indications, and that the use of diagnostic x-ray examinations be not too frequently repeated during pregnancy." While superficial investigation may reveal no apparent immediate ill effects from the radiographic exposures experienced by these pregnant women, who knows the far-flung late sequelae of such a powerful physical agent?

ETIOLOGY OF DILATATION

The characteristic dilatation of the upper urinary tract during pregnancy was noted almost a century ago by Pierre Rayer,² who commented on the finding at autopsy and the frequency with which it was associated with infection. Undoubtedly many of these cases presented an organic obstructive uropathy as a basis for their presence in the mortuary. In 1905 Opitz³ expounded the hypothesis that such dilatation was due to compression of the ureters by the enlarging uterus at the pelvic brim.

Since Opitz's time numerous observers have offered further explanation for the ureterectasis and pyelectasis of pregnancy. His mechanical theory has been corroborated by other writers. Schumacher⁴ advanced the explanation that dilatation is due to compression of the hypotonic ureter between the posterior wall of the uterus and the belly of the psoas. Carson⁵ made the

1. Miller, J. R.; Corscaden, J. A., and Harrar, J. A.: The Effect of Radiation on the Human Offspring, *Am. J. Obst. & Gynec.* **31**: 518 (March) 1936.

2. Rayer, Pierre: *Maladies des reins*, 1841.

3. Opitz: Pyelonephritis of Pregnancy and Puerperium, *Ztschr. f. Geburtsh. u. Gynäk.* **4**: 209, 1904.

4. Schumacher, Paul: Ergebnisse der intravenösen Pyelographie und röntgenologischen Suffizienzprüfung der vesicalen Ureterostien bei der Pyelitis gravidarum, *Arch. f. Gynäk.* **147**: 662, 1931.

5. Carson, W. J.: Ureteral Dilatation of Pregnancy, Autopsy Findings, *J. Urol.* **16**: 167 (Sept.) 1926.

observation on postmortem examination that the sigmoid forms a cushion for the left ureter. That the right ureter is impinged on by torsion of the gravid uterus was demonstrated by Baker and Lewis,⁶ who combined barium sulfate enema studies on the colon with their excretory urographic observations. In this



Fig. 1.—Exposure in supine position thirty minutes after injection. Patient was a primipara in the seventh month of pregnancy. Note dilatation of calices, pelvis and ureters with bilateral angulation of latter.

way the right-sided preponderance of dilatation of the urinary tract finds an apparently logical explanation.

Baker and Lewis, as well as Kretschmer and Kanter,⁷ have studied the effects of other pelvic masses in the nonpregnant woman on structure of the upper urinary tract. Such pathologic conditions as fibroids, ovarian cysts and other pelvic tumors, when strategically exerting pressure at the pelvic brim, showed characteristic dilatation of the upper ureter and pelvis, the extent and location of the lesion on the urinary tract depending on the location of the tumor and its site of greatest pressure. Both groups of observers concluded that the mechanical factor involved in these conditions mimic the situation existing during pregnancy.

Traut and McLane⁸ have shown that pregnancy alters the rhythmic peristaltic action of the ureter and that, beginning in the third month of pregnancy, a diminished amplitude of this peristaltic wave occurs, reaching its peak in the seventh month. They feel that dilatation is secondary to atony and that the etiology of the latter lies in some unexplained chemical basis rather than on any mechanical factor.

In a study of the structure and function of the ureter during pregnancy, Hofbauer⁹ noted an increase in bile salts attended with hypertrophy of the lower ureters. He demonstrated fibrosis and muscular hypertrophy in

the lower ureteral segment, attributing the dilatation above to it. Hundley and his associates¹⁰ made the same observation after anatomic and histologic study of the urinary tracts of thirteen women who died during pregnancy or at term. They found marked hypertrophy of the external longitudinal sheath of Waldeyer encasing the lower end of the ureter. They also expanded on the work of Lee and Mengert,¹¹ who performed ureteral catheter drainage on pregnant women for twenty-four hours and noted little effect on the dilatation. As a result, the latter workers concluded that the dilatation was due to some cause other than mechanical blockage. Hundley, however, wisely effected drainage for forty-eight or seventy-two hours and noted a decrease in the dilatation.

The adherents of the hormone theory claim that estrogen produces muscular hypertrophy and vascular changes while the luteinizing principle, by its relaxing influence, leads to increasing atony of the ureter. If such is the case, why is it that the degree of dilatation varies so on the two sides of the same patient? Moreover, in almost all patients no visualization of the lower ureter was noted. Any substance acting systemically should produce the same uniform effect on the entire structure.

OBSERVATIONS FROM UROGRAPHIC STUDIES

In analyzing our series of sixty patients, the observations paralleled those of previous workers in the frequency of dilatation of the upper part of the urinary



Fig. 2.—Upright exposure on same patient as in figure 1 fifteen minutes after injection. Note persistence of dilatation, nephroptosis and exaggeration of angulation of ureters.

tract starting at the brim of the pelvis, in the predilection of such dilatation to the right side and in the outward bowing or displacement of the midportion of the ureters. In only four patients was the right

6. Baker, E. C., and Lewis, J. S.: Comparison of the Urinary Tract in Pregnancy and Pelvic Tumors, *J. A. M. A.* 104: 812 (March 9) 1935.

7. Kretschmer, H. L., and Kanter, A. E.: Effect of Certain Gynecologic Lesions on the Upper Urinary Tract, *J. A. M. A.* 109: 1897 (Oct. 2) 1937.

8. Traut, H. F., and McLane, C. M.: Physiological Changes in Ureter Associated with Pregnancy, *Surg., Gynec. & Obst.* 62: 65 (Jan.) 1936.

9. Hofbauer, J. I.: Structure and Function of the Ureter During Pregnancy, *J. Urol.* 20: 413 (Oct.) 1928.

10. Hundley, J. M.; Siegel, I. A.; Hachtel, F. W., and Dunler, J. C.: Some Physiological and Pathological Observations on the Urinary Tract During Pregnancy, *Surg., Gynec. & Obst.* 66: 360 (Feb. 15) 1938.

11. Lee, H. P., and Mengert, W. F.: The Effect of Pregnancy on the Urinary Tract, *J. A. M. A.* 102: 102 (Jan. 13) 1934.

pelvis not dilated. The remainder showed pelviectasis and caliectasis varying between grade 1 and grade 4. Of these, thirty-eight showed grade 1 dilatation, ten grade 2, eight grade 3 and none grade 4. The left kidney pelvis was dilated to grade 1 eighteen times, grade 2 four times, grade 3 once and grade 4 not at all.



Fig. 3.—Supine exposure thirty minutes after injection of diodrast in multipara, aged 25. Note marked right-sided pelviectasis.

In studying the roentgenograms and the constituent parts of the urinary tract, it was noted that the left ureter was more often dilated than the pelvis of the same side. The explanation of this phenomenon may lie in the fact that left-sided obstruction is less marked than that on the right side and the degree of obstruction is insufficient, or the exposure to such an obstruction is not long enough finally to affect the corresponding pelvis. This would further support the mechanical theory. Bowing or displacement of the ureters was noted in more than 50 per cent of the patients.

Postpartum check-up excretory urograms were done as a routine on the ninth day. This usually represented the day of the mother's departure from the hospital. Rather than risk loss of the case, we chose this early date for the determination of the status of the urinary tract in the postpartum period. In only 20 per cent of our series was subinvolution noted—even after nine days (figs. 3 and 4). It is unfair to consider a patient as presenting this condition on the basis of so short an interval, since others have not noted regression to normal configuration before four weeks has elapsed.

By some fortuitous circumstance, all our patients went on to uneventful delivery. None had to be hospitalized or treated from a urologic standpoint prior to delivery. Two points are clearly demonstrated by this record: First, most women without previous obstructive lesions in the urinary tract will go through pregnancy without any lasting damage to it; Second, the vast number of pregnant women who have serious dilatation and superimposed infection are suffering from aggravation of a condition which antedated gestation. Present knowledge of the havoc raised by ureteral stone, aberrant blood vessels, constrictions at

the ureteropelvic and intramural portions of the ureter, new growths and congenital anomalies will explain, in our opinion, most instances of complications of the urinary tract in pregnancy.

Two terms often used—or misused—merit explanation. "Hydronephrosis of pregnancy" has been used to describe the condition of dilatation of the upper urinary tract during pregnancy. We do not favor the use of this term to describe a condition which, in the majority of cases, represents a transient and physiologic obstructive uropathy which returns to normal shortly after delivery. "Pyelitis of pregnancy" is another misnomer, for in practically all cases some organic obstruction is present, and infection is engrafted on the lesion (fig. 5). The systemic manifestations represent the effect of absorption of toxins from infected urine under pressure.

NEPHROPTOSIS IN PREGNANCY

Of particular interest to us was the study of renal mobility in pregnancy. Naturally we had no real criterion on which to evaluate the pregravid position and degree of mobility of the kidneys. In several cases the studies were started in the third month and in one we were fortunate in obtaining such studies in the first month of pregnancy, carried through a period of two and a half years.

Nephroptosis was found to exist in 25 per cent of our patients, varying from first degree to third degree. Those with the renal pelvis ptosed to a position opposite



Fig. 4.—Postpartum check-up on same patient as in figure 3 nine days after delivery, showing subinvolution of pelvis, especially on right side, in supine exposure taken thirty minutes after injection.

the third lumbar vertebra were considered grade 1, those opposite the fourth lumbar vertebra grade 2, and those at or below the fifth lumbar vertebra grade 4.

We noted uniformly that, as gestation progressed, the degree of ptosis was lessened, the kidney being pushed up to practically a normal position by the gravid uterus. The benefit of this work of nature is readily apparent when one notes the exaggeration of the ptosis

in the postpartum period, once the supporting influence of the enlarged uterus is removed. Ureteral angulation is then intensified and a train of symptoms associated with obstruction and hydronephrosis follows.

In one instance, pyelographic study was made on a victim of nephroptosis in her first month of pregnancy (fig. 6). Her complaint at the time was dull persistent pain in the right loin. Neither the patient nor her doctor was aware of her pregnancy at the time. Second degree ptosis was diagnosed at this time and the patient continued with her pregnancy and was observed at intervals. Her ninth month urogram (fig. 7) showed only first degree renal ptosis (pelvis opposite third lumbar vertebra), obviously corrected by the upward push of the uterus. No ureteral kink was present.

The patient's postpartum upright urogram (fig. 8) showed a return to second degree ptosis, and two and a half years later she returned for relief of a gradually increasing right-sided discomfort, and the kidney was still ptosed to a position between the fourth and fifth lumbar vertebrae. Nephropexy was performed in this instance (fig. 9). This case graphically illustrates the fate of the kidney when it shows advanced mobility.

SUMMARY AND CONCLUSIONS

With excretory urography as a basis for investigation, sixty consecutive, unselected normal pregnancies were studied. Analysis of the urograms revealed observations that coincide with those of previous observers. Progressive dilatation of the upper part



Fig. 5.—Retrograde pyelogram showing marked ureterectasis and lesser degree of pyelectasis in patient with organic ureteral (intramural) constriction. This patient, in her sixth month of pregnancy, displayed all signs and symptoms of so-called pyelitis of pregnancy.

of the urinary tract, more marked on the right side, with redundancy and lateral displacement of the ureters, was present in the majority of instances.

Special attention to renal mobility in pregnancy showed that preexisting nephroptosis was partially corrected during pregnancy but was exaggerated once the mechanical support of the gravid uterus was removed.

Such abnormal mobility also predisposes to obstruction by angulation of the ureter. In an illustrative case traced from the first month of pregnancy through a two and a half year period, nephropexy was essential for relief of persistence of symptoms.

Our own feeling regarding the etiology of dilatation of the ureter and pelvis in the pregnant state is that the problem is chiefly a mechanical one.



Fig. 6.—Upright exposure in a multipara, aged 24, in her first month of pregnancy. Note second degree right nephroptosis. Patient complained of right-sided dragging pain.

The terms "pyelitis of pregnancy" and "hydronephrosis of pregnancy" are considered misnomers. In the former, an infective process has been engrafted on some preexisting lesion, usually obstructive in nature, in the majority of instances. The latter term is a poor one to describe a condition which in the majority of instances represents an obstructive uropathy, transient and physiologic in nature, which returns to normal shortly after delivery. From our observations we would conclude that most pregnant women with no previous obstructive lesions will go through the period of gestation uneventfully, while those who do experience difficulty have had a condition which antedated gestation.

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ABSTRACT OF DISCUSSION

DR. CLARENCE G. BANDLER, New York: The graphic presentation by Drs. Woodruff and Milbert clearly narrates the story of urographic studies during and after pregnancy. This demonstration, with the work of Hundley Jr., of Baker and of the Lewis, impresses one with the rapidity of medical progress. The introduction of intravenous urography opened new fields for urologic endeavor, and, just as pediatric urology has expanded with this added impetus, so has the study of the urinary tract in pregnancy. Drs. Woodruff and Milbert have touched on a vital phase of the subject in their special attention to studies of the urinary tract in upright postures. I am well acquainted with the technic instituted by Dr. Woodruff and used by him for the past five years. One is apt to call any exposure taken with the cephalad portion of the body at an elevation of between 45 and 75 degrees an "erect exposure." This is of course

necessitated by the fact that some of the older cystoscopic tables could not be elevated higher. It is essential for proper evaluation of the position of the kidneys to make roentgenographic exposure with the patient in an erect position, his feet resting on the floor. For this purpose he leaves the table and takes a position in front of an upright movable Bucky diaphragm. In this way the natural mobility of the kidney is accurately evaluated, and the real degree of nephroptosis is ascertained. The authors have emphasized also a phase which has received no real consideration heretofore. The roentgen ray is a powerful agent and may be a very destructive one. In our enthusiasm let us not use it indiscriminately and without proper respect for the parts involved. To the urologist, the importance of such presentations as this is to show the apparent degree of urographic pathologic changes in asymptomatic, uneventful pregnancy. Opposed to the large group of normal pregnancies is the smaller one, in which, as Drs. Woodruff and Milbert have emphasized, a preexisting pathologic condition becomes subject to symptomatic exacerbation. Such illuminating reports as that of the authors stress further the need for close cooperation



Fig. 7.—Upright exposure in same patient as in figure 6 in ninth month of pregnancy. Note improved position of right kidney due to upward displacement by gravid uterus.

between the specialties of obstetrics and urology. A well trained urologist should be a valuable and active member of the staff of every obstetric service.

DR. GEORGE PRATHER, Boston: Drs. Woodruff and Milbert have presented important data concerning anatomic changes in the urinary tract during pregnancy and the postpartum period. The dilatation of the upper part of the urinary tract, which at times develops to an extraordinary degree, is apt to be interpreted as a fundamental change needing surgical correction unless one is aware of the equally remarkable return to normal which occurs in the majority of patients. In the urologic department of the Boston Lying-in Hospital a considerable number of patients have pyelographic examination both during pregnancy and several months post partum. It is my impression that, while there is a prompt change after delivery, full recovery from the hydronephrosis and hydro-ureter of pregnancy is not accomplished until three or four months after delivery. Even after four months post partum, when, as seen by intravenous pyelogram, the calices have their normal cupping and the renal pelvis has returned to a normal size, it is possible to distend the kidney by a retrograde injection of 15 or 20 cc. of fluid without pain to the patient. Such a degree of distention would not be tolerated in a normal kidney which had never been associated

with pregnancy. It is true that fundamental obstructing pathologic change in the nature of stones or aberrant vessels alters the progress of recovery, a fact which indicates the necessity of pyelograms three or four months post partum in cases of persistent infection of the urinary tract or other symptoms



Fig. 8.—Upright exposure nine days post partum showing return of right kidney to second degree nephroptosis. Check-up two and a half years later showed same situation with persistence of symptoms.

referable to the urinary tract. I do not believe that one should administer the high-powered urinary antiseptics of the present day to the patient with symptoms of long-standing duration unless one has satisfied himself that there is no anatomic patho-



Fig. 9.—Upright exposure on same patient as in figures 6, 7 and 8 one month after right nephropexy for alleviation of symptoms. Note normal position of kidney. Clinically, the patient was symptom free.

logic change destined slowly to impair renal function. As long as one realizes that a four month period post partum is advisable before deciding whether surgical correction of hydronephrosis is necessary, the chance of performing unnecessary surgical operations is reduced.

APICAL LUNG TUMORS

FURTHER OBSERVATIONS WITH REPORT OF SEVEN
ADDITIONAL CASES

JUSTIN J. STEIN, M.D.

HINES, ILL.

Malignant tumors of the thoracic inlet and pulmonary apex were first described under the heading of "superior pulmonary sulcus tumors" by Pancoast¹ in 1932. In 1924 he² first reported three cases in which certain characteristic conditions were present. At that time he referred to these cases as apical chest tumors. He later advised against the use of the name "apical chest tumor" as a designation for this type of growth, stating that it was confusing and that more common tumors would therefore be included under it.

The characteristic manifestations associated with tumors in the thoracic inlet as described by him were pain about the shoulder radiating down the arm, Horner's syndrome, atrophy of the muscles of the hand and roentgenographic evidences of a small homogeneous shadow at the extreme apex of the lung. Evidence of local destruction of ribs was always noted, and often infiltration into the adjacent vertebrae. Intrathoracic metastases were not noted. Pancoast did not believe that the tumor had its origin from the lung, pleura, ribs or mediastinum; in fact, he stated that primary lung cancer could practically be ruled out. He suggested an embryonal rest as an etiologic factor. His conclusions were based on a study of seven cases in the papers mentioned. Material for biopsy was obtained in only two and no postmortem examinations were made. The two specimens for biopsy were diagnosed as spinocellular carcinoma and metastatic carcinoma.



Fig. 1.—Appearance of chest in case 7† showing a tumor located in the right apex.

In 1937 I³ presented a paper before the section on clinical pathology before the Texas State Medical Association, reporting eight new cases of so-called superior pulmonary sulcus tumors. My object in this paper is to present additional observations made on the outcome of these eight cases and also to report seven new cases.

REPORT OF NEW CASES

CASE 1.—History.—A white man aged 45, a postoffice employee, admitted to the hospital Aug. 19, 1937, had been in excellent health until three months prior to his admission. He

stated that a cold developed accompanied by severe pain in the right upper part of the chest and shoulder region. The pain radiated down the right arm along the medial aspect to the wrist. There was marked weakness of the right arm and a loss of 20 pounds (9 Kg.). There was no history of cough, hemoptysis or night sweats.

Examination.—The patient was well developed and well nourished. Horner's syndrome was present on the right. There was some atrophy of the muscles of the right shoulder girdle, arm and forearm. A small node could be palpated just above the right clavicle. Examination of the chest revealed slight limitation of motion of the right upper part of the chest and dulness to percussion in the right apex. No rales were present. There was no alteration of breath sounds.

Urinalysis was essentially negative. The Wassermann and Kahn reactions were negative. The hemoglobin content was 80 per cent. Red blood cells numbered 4,280,000, white blood cells 9,200. Four examinations of the sputum for the presence of acid-fast bacilli gave negative results.

Roentgen examination revealed a well defined homogeneous density limited to the right apex. There was definite destruction of the medial portion of the third right rib at the costovertebral junction. An enlarged gland was seen in the right paratracheal region.

The clinical diagnosis was bronchiogenic carcinoma of the right lung, involving the upper lobe (Pancoast type).

Clinical Course.—The diagnosis was concurred in by Dr. Jerome Head, consultant in thoracic surgery, who recommended the surgical exploration. September 23, posterior segments of the upper four right ribs were resected and an extrapleural apicectomy was performed. It was impossible to separate the tumor from the spinal column, and when the pleural cavity was opened the tumor was found adherent to the apex of the lung and to the necks of the ribs and spine along the mediastinum. It was impossible to remove it. Consequently the wound was closed with interrupted catgut sutures to the muscles and fascia and silk to the skin. Microscopic examination of a specimen of the tumor removed at the time of operation was diagnosed as carcinoma, squamous cell type, originating in the lung. Palliative irradiation was advised and the patient received a total of 1,200 roentgens to the right upper part of the chest anteriorly and roentgens posteriorly. The patient received very little benefit from irradiation and was discharged from the hospital November 8. He died December 19. There was no autopsy.

CASE 2.—History.—A white man aged 50, a machine operator, was admitted to the hospital April 15, 1938, as a transfer patient from the U. S. Marine Hospital, Detroit. The patient stated that his general health had been very good until November 1937, at which time pain suddenly developed in his right shoulder, radiating down the inside of his arm to the elbow. There was some associated numbness and tingling in the third, fourth and fifth fingers of the right hand. There was some weakness of the muscles of the right upper extremity. He had lost 30 pounds (13.6 Kg.). There was no history of cough or hemoptysis. In December 1937 he went to the University of Michigan hospital where a specimen was taken for biopsy from a node in the right supraclavicular region. He was told that he had a tumor and radiation therapy was advised. He received this at the Henry Ford Hospital, Detroit. There was very little relief from the pain in the shoulder region, which was sharp in character and occurred at irregular intervals.

Examination.—The right pupil was smaller than the left, and the right side of the face was not as moist as the left side. Ptosis and enophthalmos were not present. There was a firm tumor mass in the right supraclavicular region. There was marked weakness of the muscles of the right upper extremity. Urinalysis was essentially negative. The Wassermann and Kahn reactions were negative. The hemoglobin content was 80 per cent. Red blood cells numbered 4,380,000, white blood cells 9,100.

Roentgen examination revealed a homogeneous density limited to the right apical region. Irregularity and narrowing of the superior margin of the posterior portion of the third right rib was noted. The right side of the chest was somewhat restricted.

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From the Tumor Clinic and Tumor Research Unit, Veterans Administration Facility. Published with the permission of the Medical Director of the Veterans Administration Facility, who assumes no responsibility for the opinions expressed or conclusions drawn by the author.

1. Pancoast, H. K.: Superior Pulmonary Sulcus Tumor, J. A. M. A. 99:1391 (Oct. 22) 1932.
2. Pancoast, H. K.: Importance of Careful Roentgen-Ray Investigations of Apical Chest Tumors, J. A. M. A. 83:1407 (Nov. 1) 1924.
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The clinical diagnosis was bronchiogenic carcinoma of the right lung involving the upper lobe (Pancoast type). A report of the biopsy done at the University of Michigan Hospital was medullary carcinoma.

Clinical Course.—Since the condition was considered to be of a palliative nature, further irradiation has been recommended. At the present time the patient is receiving radiation therapy. However, there has been no improvement in his clinical condition. He is remaining in the hospital for further observation.

CASE 3.—History.—A white man aged 40, a salesman, admitted to the hospital March 4, 1937, had been in good health until Nov. 1, 1936, at which time pain developed in the left knee and extended down the left leg. In December 1936 he was confined to bed because of severe pain in the entire lower left extremity. A specimen was taken for biopsy from the left femur in a private hospital and a diagnosis of osteogenic sarcoma was made.

Examination.—The patient was well developed but poorly nourished and appeared chronically ill on admission. Examination of the left lower extremity revealed no palpable enlargement. There was a scar over the anterior aspect of the thigh, which was healed.

Urinalysis was essentially negative. The Wassermann and Kahn reactions were negative. The hemoglobin content was 75 per cent. Red blood cells numbered 4,240,000, white blood cells 12,100.

Roentgen examination revealed an area of destruction in the upper portion of the shaft of the left femur, the appearance of which was suggestive of a primary bone sarcoma. Roentgen examination of the chest revealed a faint infiltration in the right infraclavicular region, which was probably the residual of an old inflammatory process.

From the biopsy at the private hospital the diagnosis of osteogenic sarcoma was made. Therefore the clinical diagnosis was osteogenic sarcoma of the left femur.

Clinical Course.—April 15, 1937, disarticulation of the left hip joint was done. The patient's postoperative condition was good and convalescence was uneventful. He was discharged August 3. He was readmitted Jan. 19, 1938, with a history that his condition had been good until October, at which time severe aching pains developed in the right shoulder region. The pain would radiate down the right arm to the elbow. Roentgen examination of the chest revealed a dense homogeneous shadow occupying the right apical region. A postoperative diagnosis of osteogenic sarcoma of the left femur with metastasis to the right apical region was made. No changes in the bony framework of the chest were noted. Many examinations of the sputum for acid-fast bacilli were negative.

Although the patient did not present Horner's syndrome, he had severe pain in the shoulder girdle with radiation of the pain into the arm, which is characteristic of an apical tumor. It is quite possible that, if he should be followed over a period of time, Horner's syndrome and possibly changes in the ribs might be observed. The patient received radiation therapy without any relief of the pain. He was discharged March 15, 1938, with the disease in a terminal condition.

CASE 4.—History.—A white man aged 37, a railway express agent, admitted to the hospital April 9, 1931, stated that he had been hoarse for approximately eight weeks prior to admission. He also complained of severe pain in the region of the left upper part of the chest. There was also a rapid loss of weight and strength, especially of the left upper extremity.

Examination.—There was a typical Horner syndrome on the left, namely miosis, anhidrosis, ptosis and enophthalmos. Examination of the larynx revealed the left vocal cord to be tense, somewhat thickened posteriorly and fixed in abduction by scar tissue. There was no evidence of any growth or active inflammation. Examination of the chest revealed dullness to percussion anteriorly and posteriorly at the left apex.

Urinalysis was essentially negative. The Wassermann and Kahn reactions were negative. The hemoglobin content was 50 per cent. Red blood cells numbered 2,800,000, white blood

cells 10,300. Numerous specimens of sputum were examined for acid-fast bacilli; however, none were found.

Roentgen examination revealed a homogeneous density involving the left apical and infraclavicular regions. There was a slight erosion of the third left rib in the posterior axillary line. There were scattered spherical densities in the parenchyma of the left lung and also enlarged nodes in the left hilus.

A clinical diagnosis was made of bronchiogenic carcinoma involving the upper lobe of the left lung with metastasis throughout the left lung.

Clinical Course.—The patient was quite ill during his period of hospitalization. Aspirations of the left side of the chest were made on several occasions and blood-tinged fluid was obtained. Examinations of the fluid for acid-fast bacilli were negative. The patient's condition became rapidly worse and he died June 2. Permission for autopsy was not granted.

This case is quite interesting in that intrathoracic metastases were present. This is the first case of this type to be reported in which intrathoracic metastases were found. Repeated examinations were made in an attempt to locate a primary lesion which would account for the pulmonary changes in this case. However, none was found, and it was therefore concluded that the tumor in the left apex was the primary lesion and the small spherules scattered throughout the left lung were considered as metastatic lesions from this left apical tumor.

CASE 5.—History.—A white man aged 40, a chauffeur, admitted to the hospital April 26, 1938, until four months prior to his admission had been in excellent health except for a chronic cough which recurred each winter. Approximately four months before

admission a severe, aching pain developed in the left arm and radiated down the inner aspect of the arm and forearm into the ring and little fingers of the left hand. The pain was quite severe and required narcotics to give relief. The pain was associated with dyspnea, cough and expectoration. The patient was hospitalized in a private institution, where a diagnosis of tuberculosis was made. Later, because a malignant condition was suspected, he was transferred to this hospital. There was considerable loss of weight and also loss of strength, especially of the left upper extremity.

Examination.—The patient was poorly nourished, appeared dyspneic and slightly cyanotic, and was acutely ill on admission. Horner's syndrome was present on the left side. There were several firm nodes present in the left lower cervical region. Examination of the chest revealed diminished expansion on the left side and also dullness at the left lower base. There was marked weakness of the muscles of the left upper extremity.

Urinalysis was essentially negative. The Wassermann and Kahn reactions were negative. The hemoglobin content was 80 per cent. Red blood cells numbered 4,250,000, white blood cells 25,700.

Roentgen examination revealed a homogeneous density in the left lung near the apex. There was a hydropneumothorax at the left base. There was no evidence of erosion or destruction of the bony framework of the chest.

The clinical diagnosis was bronchiogenic carcinoma of the left lung (Pancoast type) with metastases to the left supraclavicular region.



Fig. 2.—Appearance of chest in case 1† showing a so-called superior pulmonary sulcus tumor in the right apex.

Clinical Course.—It was necessary to perform aspirations of the chest because of the marked dyspnea caused by the pleural effusion. Bloody fluid was obtained on several occasions. Examination of the fluid did not reveal the presence of organisms. The patient's condition became rapidly worse and he died April 29.

Autopsy.—This revealed a carcinoma involving the apical portion of the left lung with metastases to the left supraclavicular region, left pleura, right lung, diaphragm, liver and mediastinal and abdominal lymph nodes. Histologic diagnosis was carcinoma of the lung, undifferentiated type, with areas simulating adenocarcinoma.

CASE 6.—History.—A Negro aged 53, a cook, admitted to the hospital Jan. 27, 1938, had been in good health until April 1937, at which time pain suddenly developed in the region of the left shoulder. The pain was sharp in character, occurred at irregular intervals and radiated down the left arm as far as the wrist. Since the onset of the pain he had gradually noticed weakness of the left upper extremity. Loss of weight was approximately

Clinical Course.—A review of the biopsy on material taken from the left supraclavicular region prior to the patient's admission to this hospital revealed a diagnosis of adenocarcinoma of the lung. Radiation therapy was recommended. However, the patient died February 21, before the treatment could be completed.

Autopsy.—There was a carcinoma occupying the left apex of the lung with extension to the left supraclavicular region and with metastases to the second and third thoracic vertebrae and the mediastinal and peribronchial lymph nodes.

CASE 7.—History.—A white man aged 39, a machinist, admitted to the hospital Feb. 8, 1938, first noticed a severe aching type of pain, which began in the right shoulder region about Aug. 1, 1937. Shortly after the pain began in the shoulder region it radiated down the inner side of the right arm into the fourth and fifth fingers of the right hand. He was seen by two private physicians and was given a diagnosis by one of neuritis and by the other of arthritis. In September 1937 he first noticed swelling in the right supraclavicular region, and a small

Summary of Fifteen Cases of Apical Carcinoma of the Lung

Case	Age	Sex	Diagnosis Prior to Admission	Chief Complaint	Wasting or Weakness of Muscles of Hand	Rib or Bone Changes	Horner's Syndrome	Lung Involved	Treatment	Result	Biopsy	Autopsy	Duration of Symptoms, Deceased Patients
1*	37	♂	Tuberculosis	Pain	Yes	Yes	Yes	Right	Surgery	Died	Squamous cell	Yes	6 months
2*	45	♂	Tuberculosis	Pain	Yes	Yes	Yes	Right	Irradiation	Died	No	Adenocarcinoma	18 months
3*	43	♂	Tumor	Pain	Yes	Yes	Yes	Right	Irradiation	Died	Squamous cell	No	15 months
4*	54	♂	Tumor	Pain	Yes	Yes	No	Right	Irradiation	Died	Squamous cell	No	32 months
5*	43	♂	Tuberculosis	Pain	Yes	Yes	Yes	Right	Irradiation	Died	No	No	15 months
6*	48	♂	Psychoneurosis	Pain	Yes	Yes	Yes	Left	Irradiation and thorotomy	Died	No	No	15 months
7*	40	♂	Neuritis	Pain	Yes	Yes	Yes	Right	Irradiation	Died	Squamous cell	Yes	19 months
8*	41	♂	Neuritis	Pain	Yes	Yes	Yes	Left	Irradiation	Died	Adenocarcinoma	No	11 months
1†	45	♂	Tumor	Pain	Yes	Yes	Yes	Right	Surgery and irradiation	Died	Squamous cell	No	6 months
2†	50	♂	Tumor	Pain	Yes	Yes	Yes	Right	Irradiation	In hospital	Adenocarcinoma
3†	40	♂	Osteogenic sarcoma	Pain	Yes	No	No	Right	Irradiation	Under observation	Osteogenic sarcoma
4†	37	♂	None	Pain	Yes	Yes	Yes	Left	Symptomatic	Died	No	No	4 months
5†	40	♂	Tuberculosis	Pain	Yes	No	Yes	Left	Symptomatic	Died	No	Undifferentiated carcinoma	4 months
6†	39	♂	Neuritis	Pain	Yes	No	Yes	Left	Symptomatic	Died	Adenocarcinoma	Yes	10 months
7†	39	♂	Neuritis	Pain	Yes	Yes	Yes	Right	Irradiation	In hospital	Squamous cell

* The first eight cases previously reported* with additional observations to date.

† These cases are reported in the text.

25 pounds (11.3 Kg.). He was told by a private physician that he was suffering from neuritis. About two and one-half months prior to his admission he first noticed a mass in the left supraclavicular region. At approximately the same time he noticed absence of sweating on the left side of his face. There was no history of cough. Slight hoarseness had been present for approximately three months.

Examination.—The patient was critically ill on admission. There was a typical Horner syndrome present on the left. There was a healed scar in the left supraclavicular region. Also a firm mass could be palpated in this region. There was atrophy of the muscles of the left shoulder girdle. The left apical region was contracted when compared with the right. There was marked weakness of the muscles of the entire left upper extremity.

Urinalysis was essentially negative except for occasional red blood cells. The Wassermann and Kahn reactions were negative. The hemoglobin content was 80 per cent. Red blood cells numbered 4,250,000, white blood cells 6,200.

Roentgen examination revealed a homogeneous density occupying the left apical region. There was slight narrowing of the intercostal spaces on the left. No costal changes were noted. There was a large node in the left paratracheal region.

The clinical diagnosis was carcinoma of the left lung (Pancoast type) with direct extension to the left supraclavicular region.

mass could be palpated at that time. Approximately three or four months before admission he noticed that there was ptosis of the right upper eyelid and that the right pupil was smaller than the left. Also there was absence of sweating on the right side of the face. There was no history of cough. Loss of weight had been 24 pounds (11 Kg.) since August 1937. There was a marked loss of strength of the muscles of the right upper extremity.

Examination.—There was a Horner syndrome on the right. A firm tumor mass was palpated in the right supraclavicular region. Examination of the lungs revealed dullness to percussion of the right apex.

There was marked weakness of the muscles of the right upper extremity.

Urinalysis was essentially negative. The Wassermann and Kahn reactions were negative. The hemoglobin content was 85 per cent. Red blood cells numbered 4,810,000, white blood cells 11,800.

On roentgen examination a homogeneous density with a well defined border involved the right apical and infraclavicular regions. There was an abnormal angulation of the second right rib posteriorly. There was also evidence of healed tuberculosis in the right lung.

The clinical diagnosis was carcinoma of the right apex of the lung of the superior pulmonary sulcus type.

Clinical Course.—A specimen was taken for biopsy from the tumor mass in the right supraclavicular region and a histologic diagnosis of carcinoma, squamous cell type, was made. The patient is receiving radiation therapy at the present time. There has been no relief from the pain.

COMMENT

An analysis of the eight cases previously reported³ with observations to date is as follows: All were white men with an average age of 43.8 years at the time of admission. The right lung was involved in six cases and the left in two.



Fig. 3.—Appearance of chest in case 47 showing an apical lung tumor in the left apex and scattered metastatic lesions throughout the left lung.

The diagnoses made prior to admission to the hospital were tuberculosis in three, tumor in two, psychoneurosis (hysteria type) in one and neuritis in two. The first symptom in every case was pain in the shoulder and arm on the affected side. Horner's syndrome was present in seven cases and costal or vertebral changes were noted in every case. Six patients were treated with radiation with no appreciable effect; one patient received both irradiation and chordotomy with very little improvement in symptoms. An attempt was made to remove the tumor mass in one case. However, because of the involvement of the mediastinum and brachial plexus, this could not be accomplished. Specimens were obtained for biopsy in five of the cases, four of which were squamous cell carcinoma and one was adenocarcinoma. All eight patients are now deceased, one patient having lived for thirty-two months. The shortest duration of life after onset was six months. The average duration of life from the onset of symptoms to death was 16.7 months. Postmortem examinations were made in three of the eight cases.

Of the seven additional cases reported in this paper, all the patients were men; six were white and one was a Negro. A primary carcinoma of the terminal bronchiole was the site of origin in six cases. The right lung was involved in four cases and the left lung in three. Pain in the shoulder girdle followed by pain radiating down the arm of the affected side was the first symptom in all cases. Horner's syndrome was present in six cases. Although Pancoast stated that the presence of Horner's syndrome was essential for the diagnosis of a superior pulmonary sulcus tumor, the time of its appearance is quite variable and depends on how early the inferior cervical sympathetics are involved. For that reason the diagnosis can be made without the presence of this syndrome if the other factors are present. Similarly costal or vertebral involvement is not essential for the diagnosis, since it may occur toward the end of the disease rather than when the patient is first seen. Costal changes were present in four of the seven cases. Histologic specimens were obtained in six cases and postmortem examinations

made in three of the four cases in which death occurred. A primary osteogenic sarcoma of the left femur with metastases to the right pulmonary apex was the etiologic factor in one case. As previously stated, it is believed that if this metastatic lesion should remain under observation and continue to increase in size, as has been noted from repeated roentgen examinations, it will probably produce Horner's syndrome and costal changes solely because of its location in the thoracic inlet rather than because of any specific properties of the tumor. Three of the patients received irradiation alone with practically no relief from pain or diminution in the size of the tumor. Surgical exploration was done in one case; however, it was found to be impossible to remove the tumor mass. Postoperative irradiation was given with no relief of pain. The average length of life after onset of symptoms in the four patients who died was six months.

SYMPTOMS

The first and most significant symptom complained of in these cases is pain and weakness affecting the parts receiving their nerve supply from the lower cervical and first thoracic nerves. The severe pain in the shoulder girdle which occurs early in the disease is a result of involvement of the origin of the posterior divisions of the first and possibly of the second thoracic common nerve trunks. The pain radiating down the inner aspect of the arm and forearm into the ring and little fingers and wasting of the interosseus muscles and those of the hypothenar and thenar regions corresponds to the ulnar nerve supply from the eighth cervical and first thoracic nerves. Horner's syndrome is a result of involvement of the inferior cervical sympathetic ganglion.

The time of appearance of Horner's syndrome and of the roentgenologic evidence of costal or vertebral changes will depend largely on the rate of growth and the mode of extension of the tumor in the thoracic inlet. The occurrence of severe pain in the shoulder girdle with radiation down the arm with or without Horner's syndrome should prompt one to make a thorough examination of the thoracic inlet both clinically and roentgenologically.



Fig. 4.—Appearance of chest in case 37 showing apical lung tumor in the right apex metastatic from an osteogenic sarcoma of the left femur.

ROENTGEN EXAMINATION

The typical roentgenographic appearance observed in these cases is a small circumscribed homogeneous density in the apex of the lung as a result of displacement of the lung.

Destruction of the posterior portions of one or more ribs and also possibly of the posterior parts of the transverse processes or sides of the bodies of the verte-

brae is generally present. These are entirely different from the roentgenographic appearances of carcinoma of the lung occurring near the hilus.⁴

HISTOLOGIC DIAGNOSES

The histologic diagnoses made from the specimens removed in twelve of the fifteen cases mentioned were six squamous cell carcinomas, four adenocarcinomas, one osteogenic sarcoma (metastatic) and one undifferentiated carcinoma with areas simulating an adenocarcinoma.

ORIGIN OF THE TUMOR

In fourteen of the fifteen cases the site of origin was definitely considered to be the terminal bronchioles of the lung. This was histologically confirmed in twelve of the thirteen cases in which biopsy material was available. Metastatic lesions from carcinoma of the breast, kidney or adrenal and from the stomach to the pulmonary apex have been reported as causing the Pancoast type of tumor; also sarcoma of the thymus, sarcomas originating near the pulmonary apex, intrathoracic sympathoblastoma, and others.⁵ By far the

patient's general condition and the size of the tumor; however, extensions occurred into the brachial plexus and mediastinum at the time of exploration. There have been reports in the literature of good results following chordotomy for the relief of pain. This was done in only one of my cases and the result was not encouraging.

2. *Irradiation.*—This method of therapy has proved to be very disappointing in this type of case. The tumors are quite radioresistant and are not complicated by secondary infections and abscesses, as compared with carcinoma of the lung in general, where definite palliative results may be obtained following irradiation, which tends to clear up the secondary infection about the tumor.

PROGNOSIS

The average duration of life of the twelve deceased patients in this series from the onset of symptoms to death was 13.1 months, one patient living thirty-two months after the onset. The shortest duration of life was four months. Because of the very unsatisfactory methods of treatment for this type of tumor, the prognosis is very poor. It is difficult to explain the rapidly fatal termination in cases of this type on the basis of the physical phenomena alone.

CONCLUSIONS

1. Further evidence shows that the majority of malignant tumors located in the region of the thoracic inlet are carcinomas of the terminal bronchioles of the lung.

2. The prognosis is very poor. The average duration of life from the onset of symptoms in this series of twelve deceased patients was 13.1 months.

3. Because of the location of these tumors in the thoracic inlet and their mode of extension to the brachial plexus and inferior cervical ganglion, surgery is not indicated.

4. Not one patient in this series received any appreciable relief from pain following radiation therapy.

5. Since severe pain about the shoulder radiating down the arm on the affected side is practically the first symptom in all cases, patients thus afflicted should be carefully examined for the other manifestations associated with these tumors in order to rule out a so-called superior pulmonary sulcus tumor.

6. Because of the symptoms, patients having apical lung tumors are generally given a diagnosis of tuberculosis, neuritis or arthritis before a tumor is suspected.

ABSTRACT OF DISCUSSION

DR. L. H. GARLAND, San Francisco: There appear to be two general types of primary pulmonary tumors of the upper lobe: those arising in the extreme apex and those arising elsewhere in the upper lobe. A significant percentage of those arising in the upper lobe spread to the adjoining rib or vertebra and the extreme apex spread to the adjoining rib or vertebra and produce erosion of bone; they press on or infiltrate the brachial plexus and inferior cervical sympathetic ganglion. When a bronchogenic carcinoma of the lung has extended to these structures, the resultant symptoms of pain in the shoulder and forearm, ptosis of the eyelid and enophthalmos permit one to make a diagnosis of "superior pulmonary sulcus tumor." Dr. Stein has pointed out that only a small number of apical bronchogenic carcinomas are associated with all these symptoms and that it is unwise to refrain from making a diagnosis of a neoplasm in their absence. It has been my privilege to see a large number of primary carcinomas of the lung in the Stanford University Medical Service at the San Francisco Hospital. Many of these have been located in the upper lobe and a few in the extreme apex; only a few of the latter have been associated

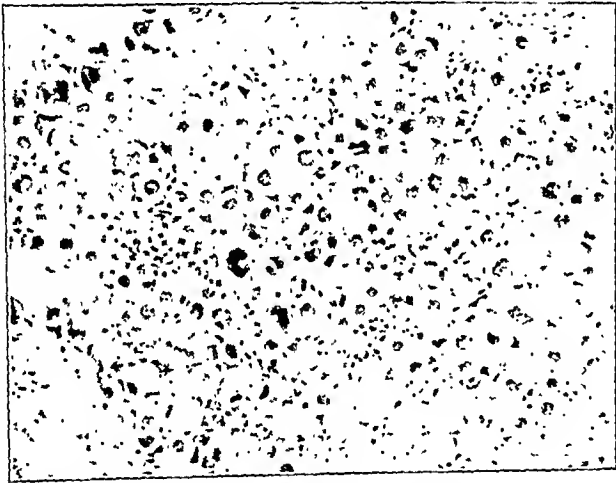


Fig. 5.—Section from tumor in case 71 showing a grade 4 carcinoma, squamous cell type.

majority of cases reported have been atypical carcinomas of the lung.³ I am of the opinion that these tumors are more common than is generally realized. Since 1936 thirteen so-called superior pulmonary sulcus tumors have been diagnosed at the Hines hospital, all of which have been carcinomas of the lung. More than forty-four cases have been reported in the literature by various authors during the past six years.

TREATMENT

1. *Surgery.*—Because of the location and the mode of extension of these tumors, it is impossible to remove them surgically. Although the tumor may be quite small when seen on the roentgenographic film, extension into the brachial plexus and into the mediastinum will generally be found. Two of the cases in this series were excellent surgical risks from the standpoint of the

4. Stein, J. J., and Joslin, Hope L.: Carcinoma of the Bronchus, Surg., Gynec. & Obst. 66: 902-911 (May) 1938.
S. Evans, W. A., in discussion on Pancoast, Tobias, J. W.: Syndrome apico-costovertebral doloroso por tumor apical: Su valor diagnóstico en el cáncer primitivo pulmonar, Rev. méd. latino-am. 17: 1522-1556 (Aug.) 1932; 18: 304 (Dec.) 1932. Frost, T. T., and Wolpaw, S. E.: Intrathoracic Sympathoblastoma Producing the Symptomatology of a Superior Pulmonary Sulcus Tumor (Pancoast), Am. J. Cancer 26: 483-492 (March) 1936. Browder, Jefferson, and DeVeer, J. A.: Varied Pathological Basis for Symptomatology Produced by Tumors in Region of Pulmonary Apex and Upper Mediastinum, Am. J. Cancer 24: 507-521 (July) 1935.

ciated with the classic symptoms originally described by Pancoast. Because of the manifestations in these cases and the absence of a significant number of nonbronchogenic neoplasms producing such symptoms, I am inclined to agree with Browder, De Veer and the author that it is unwise to classify tumors on a basis of location and that if adequately studied most of the "superior sulcus tumors" will be shown to be either bronchogenic carcinomas or tumors of the lower cervical lymph nodes. I have observed one case of Hodgkin's disease of the supraclavicular lymph nodes in which all the signs of a so-called superior sulcus tumor were present. In a previous paper Dr. Stein pointed out that the differential diagnosis in cases in which there are symptoms produced by invasion of or pressure on the brachial plexus, erosion of ribs or vertebrae and changes in the sympathetic nerves includes cervical rib, aneurysm, apical tuberculosis, primary or metastatic tumors of the cervical lymph nodes and primary or metastatic tumor of the pulmonary apex. However, Dr. Stein believes, and probably correctly, that in the majority of cases it is bronchogenic carcinoma that produces such symptoms. The two interesting points brought out by Dr. Stein in his present analysis of fifteen cases are the relatively low average age of the patients, 43 years, and the constancy of the presenting symptoms of pain in the shoulder and arm on the affected side.

DR. JUSTIN J. STEIN, Hines, Ill.: Regarding the question of the use of higher doses in cases of this type, I have given as high as 6,000 roentgens without producing any appreciable palliative effect. Many of the patients ask that radiation therapy be discontinued because no improvement can be noted and because a reaction about the brachial plexus causes more pain. In the radiation therapy of carcinoma of the lung, in general I give relatively small total doses, because I believe that all the radiation therapy accomplishes is lessening of the secondary infection and abscess formation about the tumor and possibly some diminution in the size of the tumor. As the secondary infection is lessened the patient's clinical condition is improved. I have not noted the presence of infection about tumors in the apical region, and this may account for the fact that practically no improvement follows the administration of radiation therapy in cases of this type. This group of fifteen cases of tumor of the apex was selected from 200 cases of primary carcinoma of the lung that were observed at the Veterans Administration Facility since 1931.

DR. JOHN MURPHY, Toledo, Ohio: May I ask Dr. Stein to enlarge a little on the method with which he gave this large dose?

DR. STEIN: I use a 10 by 10 cm. portal, from 80 to 100 target skin distance, 2 mm. of aluminum, 1 mm. of copper, from 15 to 20 milliamperes and 200,000 volts.

DR. MURPHY: But the daily dose?

DR. STEIN, Hines, Ill.: The daily dose is 200 roentgens given through two or three portals, alternating the portals.

Sterilization of the Feeble-minded.—Sterilization of the feeble-minded had been urged as a preventive measure in America even before the present century was ushered in. As early as 1897 Dr. M. W. Barr, in his presidential address before the American Association for the Study of Feeble-mindedness, strongly advocated it as the most practical step in a preventive program. In the same year the first human sterilization bill in this country was introduced in the Michigan legislature but failed of passage. Indiana was the first state to enact a human sterilization law. This pioneer statute, passed in 1907, provided for the compulsory sterilization of "confirmed criminals, idiots, imbeciles and rapists." The operation was to be performed after a committee of experts and institutional officials had decided that procreation was inadvisable and that there was no probability of the subject's mental improvement. Later laws in Indiana modified the administrative details of the original statute and extended the scope of sterilization to noninstitutional mental defectives upon the recommendation and approval of the proper authorities.—Deutsch, Albert: *The Mentally Ill in America*, New York, Doubleday, Doran & Co., Inc., 1937.

THE TREATMENT OF CANCER OF THE EYELIDS

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Preservation of tissue and function is seldom considered with greater care in the treatment of cancer than for growths on the eyelids. By the present methods of radiation therapy cancer in this location may be destroyed with minimum loss of normal tissue and consequently without deformity other than that caused previously by the growth itself.

From 1932 to 1937 inclusive, sixty-two consecutive patients with cancer of the eyelids were treated. Positive results from biopsy were obtained for forty-eight patients, and only this group will be considered in this discussion.

ETIOLOGY

Chronic irritation is an important inciting factor for the majority of cancers of the eyelids. A local causative factor, namely eyeglasses, was demonstrated definitely with fourteen patients. The nose piece, either ill fitting or worn and rough, was a factor with eight patients, since the growth started in the depression or on the margin made by the guard. Pressure of the glasses also may contribute to the development and progress of other growths in this vicinity by diminishing the blood supply. With six patients the frame of the glasses or the edge of the glass itself rested on the skin of the lower eyelid and neoplasm developed in the irritated area.

Burn scars of variable duration were causative factors in three cases. One burn was from gasoline and occurred fifteen years previously; the scar became irritated by glasses and ulcerated. Another burn occurred twenty years previously as a result of an ether explosion; the scar broke down for no apparent reason. The third burn was from hot grease and occurred two years previously, and the wound did not heal.

One patient gave an unusual history of having at least fifty styes on each eyelid. The scars from continued infection may easily have altered the skin and blood supply and thus acted as an inciting factor.

Other contributory factors of a constitutional or more general nature must exist, since eighteen patients, or one third in the series, had one or more cancers on the skin of the face in addition to the growth on the eyelid. I found that many of this group were in direct contact with oil and its derivatives. That the face and eyelids had been rubbed with hands soiled with various coal tar products was frequently brought out in the histories. One patient cleaned wood and coal stoves with crude oil and gasoline for forty years. Fifteen years after this exposure he had eighteen cancers on the skin of his face alone and one on an eyelid. The second most frequently encountered factor was sunlight and the elements. Many patients were occupied during their active lives with work requiring them to be exposed to sunlight and all weather conditions. The histories of the eighteen women in this series were not contributory.

Read before the Section on Ophthalmology at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 17, 1938.

The incidence is greater for men. This series includes thirty men and eighteen women. The majority of patients were elderly, and thirty-four, or 70 per cent, were 60 years of age or older. The oldest patient was a woman of 91, who had a squamous carcinoma near the inner canthus of the lower eyelid. The youngest patient was a man of 24, with a squamous carcinoma involving the lower eyelid a few millimeters from the tarsus.

PATHOLOGY

A determination of the site of origin was difficult with the majority because of the extent of the growth at the initial examination. In all probability the mucocutaneous juncture was the common site (as on the lip), where the factors of irritation are most evident. The skin of the eyelid was demonstrated as the original site in nine cases, and the histories in this group were not contributory. In eight cases the growth originated in one canthus of the eyelids. The inner canthus and the lower eyelid were most commonly affected; the disease is less frequently seen at the outer canthus and on the upper eyelid, although in four cases in this series the cancer was observed on the upper lid. Four growths originated in or near the opening of the lacrimal duct.

Two patients had more than one growth on the eyelids. Two squamous cancers occurred on the upper eyelid of one patient. A basal cell cancer involved the outer canthus of the right eyelids and the inner canthus of the left eyelids. Multiple cancers on the skin of the face in addition to the growth on the eyelid were observed in eighteen cases, or approximately one third of the series.

The pathologic structure of neoplasms on the eyelids was fairly uniform. The basal cell type occurred in thirty-eight cases and the squamous type in eight cases, and in one case the growth had both basal and

a false impression of the actual size may result unless the elastic, smooth, translucent thickening around the ulcer is clearly apprehended. The periphery of the tumor may be entirely free of the overlying skin, and this type is always radiation sensitive; such swellings disappear very rapidly when they are treated by either external or interstitial radiation.



Fig. 2 (case 1).—An extensive, superficial basal cell growth of the eyelids treated by external irradiation.

The squamous cancer is more aggressive and destructive. It may begin as a hypertrophic, warty growth which undergoes necrosis in the center early, or as a nodule or fissure. Invariably ulceration appears early in the form of a flat, superficial ulcer with hard, everted edges. It is more apt to invade and destroy the tissues, and, potentially, the squamous growth is capable of producing metastases to regional lymph nodes, although no metastasis was demonstrated in this series. The preauricular or upper deep cervical lymph glands are the first affected when metastasis does occur.

SYMPTOMATOLOGY AND DIAGNOSIS

Early signs and symptoms were not uniform, and recognition was difficult. A hypertrophic wart, crust, flat superficial ulcer or fissure or a fine, granular ulcerated nodule was the first sign observed by twenty-four patients. In all probability the majority of these patients passed through a precancerous keratotic stage. A hypertrophic, warty growth with intermittent crusting is regarded as a precancerous lesion and should be considered suggestive of early malignant changes. A lump or nodule was first observed by twelve patients, and their meaning for this term included thickening in the skin, styes and cysts. Three patients observed a cyst first, and one patient stated that it was present for twelve years without change before activity was observed. Five patients observed a pimple that progressed in spite of the customary attentions. Four patients described a small pigmented mole that became active.

The typical appearance of a growth on the eyelids is similar to one on the skin elsewhere. The majority, and especially the basal cell type, begin as a semi-transparent nodule with a depressed center, which subsequently breaks down to form an ulcer. A crateriform appearance is common. The raised, rolled margin is pearly, and an impression of the depth of invasion may be gained by the edge, which is usually undermined and indurated. The ulcer progresses and if untreated spreads both laterally and in depth, destroying all tissues

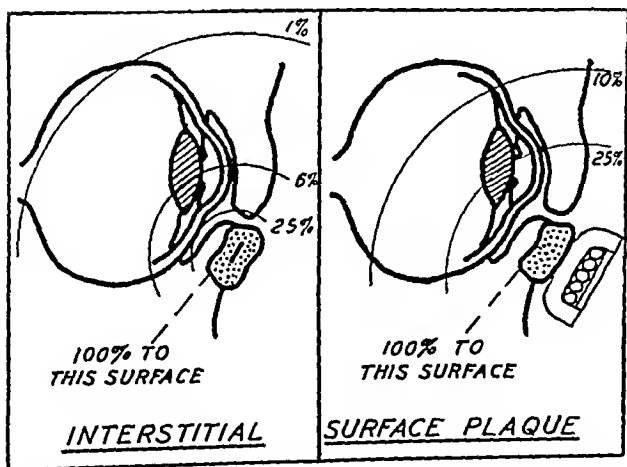


Fig. 1.—Relative distribution of radiation intensities in radium treatment of cancer of the eyelid. Diagrams showing doses delivered to the growth by interstitial and external irradiation. Note the relative doses delivered to the surrounding tissues by the two methods of application, as indicated by the iso intensity lines.

squamous characteristics. A metastasis to the eyelid occurred in one case from a cancer of the pancreas. Three cancers started in the adjacent skin and involved the eyelid secondarily.

The basal cell type progresses by direct extension and burrows into the deeper layers of the skin and the subcutaneous tissue. The ulcer itself usually does not enlarge in proportion to the growth of the tumor, and

in its path. Other growths arise in cysts or in the base of hair follicles and may not be ulcerated, but their dome-shaped appearance with a pearly glaze may be of diagnostic value. The induration is the same, and if the surrounding tissues are involved the rolled edge is evident. Occasionally the basal cell growths appear brownish because of pigment, but this color is usually lost when they become ulcerated.

The duration of the history of the signs or symptoms parallels roughly the size, rather than the type, of the growth. The age of the patient likewise was not consistent with the duration of the lesion, although the youngest patient, a man aged 24, had a squamous growth of only two months' duration. Other patients had an equally short history; for example, a man aged 84 had a basal cell cancer of the same size, also of only two months' duration. The longest history was fourteen years, and the average duration before treatment was twenty months.

Symptoms are negligible except when the growth has invaded the conjunctiva; then foreign body symptoms result, and inflammation, excessive lacrimation and photophobia usually follow. Involvement around the orifice of the lacrimal duct may obstruct it and cause lacrimation. Pain was not mentioned by any one in this series even though many growths were large and several were attached to the periosteum. Involvement of the canthus may cause inflammation of the lids and pain on movement.

After a complete description and examination of the growth, a positive diagnosis can be made only by a microscopic study of biopsy material taken from the growth. Differentiation between a benign and a malignant process is the first consideration. Whether the malignant growth is squamous or basal cell cancer must be established entirely by the microscopic study.

TREATMENT

Irradiation procedures are employed successfully in the treatment of cancer of the eyelids. The effective, or cancerocidal, dose is calculated according to the

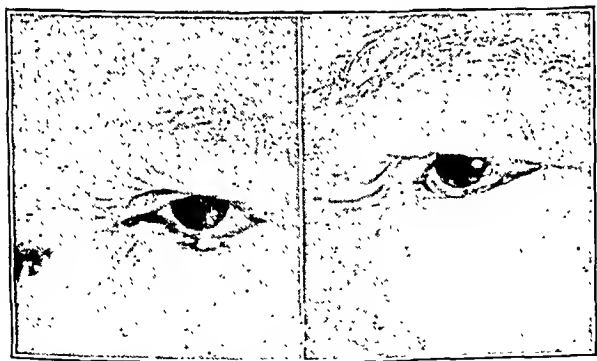


Fig. 3 (case 2).—A superficial basal cell growth treated interstitially.

dimensions and histologic type of the growth. The radiation is delivered either by a surface application of radium or interstitially by means of radium needles or radon seeds; in the majority of cases a combination of surface and interstitial irradiation will give the best cosmetic result. Decision for the selection of these procedures depends on the location, proximity to bone, involvement of the lacrimal duct or sac, degree of invasion and adaptability of the procedure for the individual case. By carefully controlled irradiation

complete regression of the growth may be expected with a minimum deformity and without late radiation damage to surrounding structures.

The physical factors involved in planning radium treatments include filtration, distance from source to skin, protection of surrounding tissues and in the case of radon the rate of decay of the source.



Fig. 4 (case 3).—Invasive basal cell growth which was treated by surface and interstitial radium therapy.

The filtration in every case is sufficient to remove all the beta rays, which are very active destructive agents and if not removed by sufficient filtration often result in damaging necrosis.

The greater the distance from the source (or applicator) to the skin, the greater will be the percentage of the skin dose which will be measured at a given depth below the skin. By increasing the source-to-skin distance, the actual absolute intensity is decreased, but the relative depth effect is increased. In the series here presented the applicator was placed directly on the skin.

The lead protection for the eyeball and crystalline lens may be placed at the eye, under the lid or at the plaque itself. In the interests of the patient's comfort this protection usually took the form of a 2 mm. lead screen applied to the portion of the applicator from which would emanate the rays which would reach the tissues to be protected. The protective screen is shown in figure 1 as it reduces the intensity according to isodose lines in the chart.

Application of the inverse square law of decrease of intensity from the source serves as the best protective measure for interstitial needles or radon seeds. Since the intensity decreases with distance from the source, their greatest activity is immediately surrounding them. For this reason they are injected directly into the growth. Normal surrounding tissues are automatically protected by the decrease in intensity with distance.

The anatomic architecture and geometric considerations in the individual case to a large extent determine the choice of the physical variables, such as filtration, distance and protection.

From 1932 to 1937 inclusive, forty-eight patients for whom biopsy showed cancer were treated. Treatments according to years were as follows: 1932, three patients; 1933, four; 1934, eight; 1935, eight; 1936, nine, and 1937, sixteen. The procedures were varied widely in order to meet the requirements for each particular growth.

Fourteen patients in the series had recurrences after previous treatment. Six had been treated only once

before, two by an electric needle and four by low voltage roentgen therapy. The remaining eight patients had been treated more than once by various means, such as the electric needle, cautery, surgical intervention and freezing. The scarring which followed such procedures caused considerable deformity in many instances, and the irradiation problem was more difficult than for the uncomplicated and untreated growths.

Postoperative Irradiation.—Exeision was performed for diagnosis as well as treatment on three growths which were small, nonulcerated and clinically without positive diagnosis. Two of the three were near the tarsus, and postoperative interstitial irradiation was done when the wounds healed. The scars were less than 1 cm. in length, and two 2 mg. radium needles having a filtration value of 1 mm. of platinum were placed under them for a total dose of approximately 300 milligram hours.

Surface Irradiation.—The application of radium on the surface of a growth demonstrates its radiation sensitivity and the selective effect toward radium most clearly. Topical radiation was the only treatment given



Fig. 5 (case 4).—An aggressive basal cell cancer which involved both eyelids and the periosteum at the margin of the orbit. Destruction of the growth was accomplished by combined surface and interstitial radium therapy without deformity.

eighteen patients. The growths receiving this type of treatment were superficial and at a distance from the tarsus. Lesions near the lacrimal duct were also included in this group, in order to avoid unnecessary fibrosis and distortion. A small square plaque (2.5 cm. by 1 cm.) containing 25 mg. of radium and 2 mm. of brass filtration was the common applicator for growths 1 cm. in diameter or less. A protection of 2 mm. of lead was fastened along the surface of the plaque nearest the lens. The application was made directly on the surface of the growth, and a dose of from 450 to 650 milligram hours was delivered in one treatment. The reaction appeared ten days later and persisted for three or four weeks. Healing should be retarded by applying ointments, yellow mercuric oxide (1 per cent), boric acid ointment or white petrolatum. Gauze patches with the ointment retard healing even further, until the primary site is smooth and the skin is permitted to grow over the area slowly, without contraction.

Interstitial Irradiation.—Treatment by radium needles or radon seeds was the only treatment given sixteen patients. All those with squamous cancer were included in this group and certain of those who had cancer of an aggressive basal cell type which demonstrated growth at a depth but with a diameter of less than 1.5 cm.

As before mentioned, several of the patients had been treated previously by various destructive agents, and recurrences were found in the scars. The growth, either basal cell or squamous, is more resistant in scar tissue, and the radiation is more effective when applied interstitially. Removable radium needles are preferable to radon seeds because there is less scarring and because no foreign bodies are left in the tissues. Not infrequently the radon seeds prolong the reaction unnecessarily by their presence, and many times they must be removed some months later. Radium needles containing 2 mg. of radium with a filter of 1 mm. of platinum were used for this group. The needles were placed directly under the growth in most instances, horizontally, a few millimeters apart. As many needles were implanted as was practicable for the most efficient irradiation, so that the duration of exposure was a minimum. The dose was calculated according to the type and dimensions of the growth, the special requirements of recurrent growths in scar tissue being taken into consideration. The average treatments were from 350 to 700 milligram hours.

Swelling of the lids occurred with the insertion of the needles, and this usually persisted to a varying degree throughout the reaction period of from four to six weeks. The reaction was similar in all respects to the effects after external irradiation.

Combined Surface and Interstitial Irradiation.—A preliminary surface application of radium followed by interstitial therapy is necessary for most growths over 1.5 cm. in diameter and also for those which invade either the surrounding structures to a considerable depth or the orbital tissues. The application of both external and interstitial sources of radium enables the therapist to avoid unnecessary changes in the skin or subcutaneous tissues. The total dose and the fraction assigned to each method of treatment is dependent on both the diameter of the growth for the surface therapy and the depth of invasion for the interstitial treatment. Approximately one third of the total dose was delivered by an external source and two thirds by interstitial application of radium needles or radon seeds. Eleven patients were treated by the combined methods. Although their growths were the most extensive in the series, the reactions were not greater in severity and duration than those that followed the single procedures for the smaller growths.

The various procedures in this series of cases were primarily successful, with the complete disappearance of the growth in all instances. All the patients have been followed to the present time except one who was treated in 1935 and was followed for eight months. Seven patients died of intercurrent disease without evidence of recurrence or metastasis. The remaining patients (forty) are free from disease, but for only eighteen of these has three years yet elapsed after the last treatment.

The prognosis for cancer of the eyelids is excellent when irradiation is used, and one may expect complete regression of the cancer, with a minimum deformity and rare late radiation effects in the lens, cornea, conjunctiva or skin.

REPORT OF CASES

CASE 1.—W. C. C., a man aged 65, a carpenter, examined Aug. 9, 1937, complained of a growth on the eyelid and one on the ear. Ten years previously a small lump appeared below the inner canthus of the eye. It was itchy and frequent irritation

caused it to open, and growth was gradual to the present size. From the site of onset the growth involved the lids by direct extension. Symptoms of conjunctivitis and excessive lacrimation had been annoying during the past few weeks.

On examination a nodular, ulcerated growth 3.5 cm. in its longest diameter was seen involving the inner canthus of the right eye and the medial fourth of both eyelids. It infiltrated the full thickness of the eyelids, and the conjunctiva on the under surface of the lids was involved. The growth surrounded the



Fig. 6 (case 5).—Involvement of three-fourths of the lower eyelid with invasion of the conjunctiva and orbital tissues. Combined surface and interstitial therapy was necessary to destroy the growth by radiation with minimum deformity.

tear duct and extended down to the lacrimal sac, with possible early invasion of the sac. The skin on the side of the nose as well as down over the cheek was extensively involved. The left auricle was partially destroyed by the same type of growth. The specimen taken for biopsy showed the presence of basal cell carcinoma.

On August 10 a rectangular plaque (2.5 cm. by 1 cm.) containing 50 mg. of radium with 2 mm. of brass filtration was applied over three areas directly on the surface of the growth. A protection of 2 mm. of lead was fitted to the ocular side of the plaque. The applications consisted of one over the inner canthus, one on the nasal portion and another on the facial portion. The inner canthus received 800 milligram hours, and the other areas were given 600 milligram hours each.

The reaction was acute, and the patient's discomfort was alleviated with yellow mercuric oxide (1 per cent) or white petrolatum for the conjunctival reaction and with boric acid ointment for the skin. The area was entirely healed in two months, and now there are no symptoms and no deformity or impaired movement of the eyelids.

CASE 2.—W. J., a man aged 76, a farmer from Texas, first seen Nov. 16, 1934, complained of a sore on the lower eyelid. The skin of the face had always been sensitive, and previously several growths had been treated by desiccation and low voltage roentgen therapy. Eight months previously a growth appeared on the eyelid similar in onset to those elsewhere on the face. Enlargement was gradual to the present size.

On examination an ulcerated growth 1.5 cm. in diameter was seen involving the midportion of the left lower eyelid. The edges were rolled, and it widened the lid by direct invasion. Early involvement of the conjunctiva had already taken place. The tarsus was involved and partially destroyed. The biopsy specimen showed a basal cell carcinoma.

Two 2 mg. radium needles with 1 mm. of steel filtration were inserted November 22 beneath the growth, one at each end. A dose of 160 milligram hours was given.

A very acute local reaction followed, with conjunctivitis, lacrimation and photophobia. The area healed in six weeks, and there is no discomfort, deformity or impaired vision now, nearly four years after treatment.

CASE 3.—H. B., a housewife aged 75, first treated March 26, 1936, had first observed a small pimple in 1933. It had enlarged gradually until six months previously, when she scratched and opened it. Growth had since been rapid.

On examination an ulcerated growth 2 cm. in diameter was seen involving the outer half of the right lower eyelid. The crater of the growth was several millimeters below the surface of the skin, and the full thickness of the lid was invaded. The margin of the lid was distorted because of involvement of the tarsus. The biopsy specimen showed a basal cell carcinoma.

On March 26 a radium plaque (1.5 cm. by 1 cm.) containing 25 mg. of radium with a 2 mm. brass filter was applied on the surface. A protection of 2 mm. of lead was fitted on the upper surface of the plaque, and a dose of 400 milligram hours was given. On March 30 four 0.3 mm. gold seeds containing 1.2 millicuries of radon each, or a total of 4.8 millicuries, were inserted.

The patient had little discomfort, and at present, over two years later, there is no deformity of the lid and no complaint of dryness or impaired vision.

CASE 4.—O. W. S., a man aged 62, a broker, examined Aug. 2, 1932, complained of a sore on the eyelids. A small pimple was first noticed at the outer canthus of the right eye six years previously. It grew gradually into a dome-shaped tumor that involved both eyelids. One year previously it ulcerated and doubled in size.

On examination a crater-like growth 2 by 1.5 by 1 cm. in diameter was observed at the outer canthus of the right eye. It involved the upper and lower lid equally and infiltrated through the thickness of the lids, but the conjunctiva was not ulcerated. The growth was attached to the periosteum, and early invasion of the lateral tissues of the orbit was evident. The biopsy specimen showed a basal cell carcinoma.

On August 2 a rectangular radium plaque (2.5 cm. by 1 cm.) containing 50 mg. of radium with 2 mm. of brass filtration was applied vertically on the surface. A protection of 2 mm. of lead was fitted to the ocular side of the plaque, and a dose of 1,000 milligram hours was given. On August 11 two 0.3 mm. gold seeds containing 1.5 millicuries of radon each were inserted, one into each eye.

The reaction was acute; photophobia persisted for six months, and this sensitivity recurred in 1934. At present, over five years after treatment, there is no evidence of disease, photophobia or lacrimation. The lateral part of the conjunctiva is whitened and at times dry. Vision is not impaired in the eye.

CASE 5.—G. N., a woman aged 37, a housewife, first seen May 12, 1935, complained of a tumor of the eyelid. In 1922 a lump first appeared on the eyelid; it was desiccated soon after the



Fig. 7 (case 6).—Destruction of the inner fourth of both eyelids and involvement around the lacrimal duct. Complete destruction of the growth was accomplished by the combined applications of radium without deformity or destruction of the lacrimal duct.

onset. A recurrence appeared, and desiccation was attempted again in 1925 and 1928. An operation was performed in 1930; the wound failed to heal, and there was gradual growth to the present size.

On examination an ulcerated crater-like growth 2.5 cm. in diameter was observed extending down from the free margin of the left lower eyelid. It infiltrated through the full thickness of the lid, and the tarsus appeared invaded or at least surrounded. When the lid was drawn down the growth showed early

invasion of the conjunctiva, and there were two minute ulcerations. The growth moved over the maxilla even though there was invasion along the floor of the orbit. A biopsy specimen showed basal cell carcinoma.

On May 12, 13 and 14 a plaque (1.5 cm. by 1 cm.) with 25 mg. of radium and 2 mm. of brass filtration was applied on the medial and lateral halves of the growth directly on the surface. A protection of 2 mm. of lead was fitted along the upper surface of the plaque, and a dose of 900 milligram hours was given over each area, or a total of 1,800 milligram hours by external irradiation. The reaction appeared on May 22 and soon became acute. On August 16 five 0.3 mm. gold seeds containing 0.8 millicurie of radon, or a total of 4 millicuries, were inserted, two along the floor of the orbit and three along the tarsus.

The radiation reaction was intense, with lachrimation and photophobia. At present, three years later, there are no complaints of lachrimation, dryness, photophobia or impaired vision.

CASE 6.—M. M., a woman aged 62, a housewife, first seen on Jan. 4, 1934, complained of a sore on the eyelids. Two years previously she was burned with grease, which broke her glasses and burned her eyelids severely. The burn healed slowly to an area a few millimeters in diameter and then gradually opened to its present size. The patient attributed the lack of healing to the glasses, which rested directly on the sore.

On examination an ulcerated growth 2.5 by 2 by 0.4 cm. in diameter was observed at the inner canthus of the right eye. It infiltrated the inner part of both lids and extended over on the bridge of the nose to the midline. The full thickness of the skin was involved, and the growth moved over the periosteum. There was involvement up to the lacrimal duct, but there was no induration around it. The biopsy specimen showed basal cell carcinoma.

On January 6 a rectangular radium plaque (2.5 cm. by 1 cm.) containing 50 mg. of radium with 2 mm. of brass filtration was applied horizontally on the surface. A protection of 2 mm. of lead was fitted to the ocular end of the plaque, and a dose of 950 milligram hours was given. On February 19, after the acute reaction had subsided, three gold seeds were inserted, each containing 1.3 millicuries of radon. One radon seed was placed above the inner canthus, one below and the third still deeper along the medial wall of the orbit.

The reaction became acute again and persisted until the third week of March. The irritation subsided slowly, and now, over four years subsequent to treatment, there are no symptoms of dryness, excessive lachrimation or visual changes and no deformity.

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ABSTRACT OF DISCUSSION

DR. EVERETT L. GOAR, Houston, Texas: The subject is one not often discussed before ophthalmologists, probably because few ophthalmologists attempt to treat cancers of the eyelids. We are as much in the dark about the cause of these growths as we are of cancer elsewhere. Chronic irritation undoubtedly plays a part and perhaps the reason the lesion appears oftenest at the inner canthus is that it is most bathed by excessive tears or secretion. The guards of eyeglasses may cause irritation on the skin of the nose which could easily involve the eyelid by extension, but as for eyeglasses initiating a growth within the lid itself, I doubt that it is possible. It has been my custom to refer patients in whom I suspected a malignant lesion of the eyelids to a dermatologist for treatment. I do not believe that treating these lesions surgically serves the best interest of the patient. It is true that these growths can be removed safely and surely by wide excision, by cautery or by fulguration, but the loss of tissue and subsequent scarring are undesirable. Many a patient has been subjected to a plastic operation on the eyelid who would not have needed it if the neoplasm had been treated primarily by radium. Dr. C. M. Griswold has furnished me with statistics of patients treated by him during a ten year period. His records show 208 cases of cancer of the eyelids in 136 males and seventy-two females. One hundred were at the inner canthus, twenty-four at the outer canthus, sixty-eight

in or near the central area of the lower lid and sixteen in or near the central area of the upper lid. Five of the patients were under 30 years of age but the vast majority were 50 or over. About 5 per cent of the cancers were of the squamous cell type, while 95 per cent were basal cell or basosquamous. All these patients were treated by the topical application of radium, with an average of 550 mg. hours. There were eight failures in the group. Most of the remainder have been followed for a varying period of from one to ten years and are satisfactorily healed. Cicatricial ectropion has not occurred as a complication from the treatment, but in five cases in which the lesion had perforated the lid and the conjunctiva was involved, symblepharon developed. No irradiation cataract has been noted in the series. All patients had a permanent loss of lashes on the affected lid. Dr. Griswold has used the same technique throughout the series. A 2 mm. lead mold which is wrapped in pure gum rubber to prevent secondary irradiation is placed between the radium and the cornea. The radium plaque, encased in a 0.5 mm. platinum shield, is applied directly to the lesion. Three or four applications are made within a week. In the majority of early cases this has caused the lesion to disappear within six or seven weeks, leaving a thin, pliable scar that is scarcely visible.

DR. DOHRMANN K. PISCHEL, San Francisco: Many ophthalmologists have felt that, when possible, surgical excision of small epitheliomas is the simplest and quickest method for dealing with these tumors. If small, this appears to me to be quite correct. If the surgical procedure is properly planned and executed, no deformity will result and the convalescence is short and comfortable. However, the small lesions that are amenable to surgery are also most amenable to irradiation and I myself feel that irradiation is the method of choice in such radio-sensitive tumors as Dr. Sharp has described. Unfortunately, these cancers are most often seen when in a late stage, and here surgical treatment is impossible. It is interesting, therefore, to see the excellent results that can be achieved by radiation therapy. It must be emphasized that such excellent results are not to be obtained by careless work. The whole procedure must be carefully planned and carefully carried out. Haphazard irradiation will produce incomplete results or, what is worse, marked deformities. Even at best, some occasional atrophy of the lids may result, with ectropion, entropion or trichiasis. These situations can usually be successfully remedied by simple plastic procedures. This must be qualified by the statement that those procedures are simple if properly executed.

DR. OTIS A. SHARPE, San Francisco: I report a case that was not treated with radiation. I present it because of the radical prophylactic procedure against metastasis. The patient presented herself at the clinic in February 1932 complaining of a small lump in the middle of the right upper lid. She stated that she had had something on this lid, which she described as a pimple, for some months, but that in the last few weeks it had grown rapidly. The growth was the size of a large garden pea. Both upper and lower lids were removed, the orbit exenuected, and a graft applied to the orbit. The pathologist's report on biopsy was basal cell carcinoma with very little evidence of mitosis. The patient presented herself at the clinic in February 1937 complaining of severe pain in the legs, in the pelvic region and in the lumbar region. X-ray studies revealed large punched out areas which had destroyed the larger portions of the bones of the pelvis and the upper fourths of the femurs, definitely involving the lumbar vertebrae. The right half of the diaphragm was found to be elevated, suggesting a tumor mass anterior to the diaphragm, possibly the liver. There were no definite metastases to the lungs. The skull showed no irregular osteoporosis. The areas of decreased density were not punched out as one would expect with a multiple myeloma. There was some thickening of the cranial vault. The upper end of the sternum appeared to be somewhat cystic in character similar to changes seen in the pelvis. A biopsy specimen was taken from the sternum and examined by another pathologist along with the first pathologist and the microscopic pictures of the two, viz. the original lid tumor and the sternum sections, were found to be identical.

FOCAL INFECTION: QUARTER CENTURY SURVEY

FRANK BILLINGS LECTURE

WALTER L. BIERRING, M.D.

DES MOINES, IOWA

It seems particularly fitting that the annual lecture-ship established by the Section on Practice of Medicine should commemorate the name of Dr. Frank Billings. His eminent leadership influenced in a large measure the development of this and other scientific sections of the Association. Furthermore, in the field of medical education and as a builder of medical schools, hospitals and research institutes he left an enduring impress on American medicine.

Of his many contributions to clinical medicine the most outstanding is the modern concept of focal infection as related to chronic systemic disease, which was first presented in his classic article¹ entitled "Chronic Focal Infections and their Etiological Relations to Arthritis and Nephritis."

In the passing of a quarter of a century the many implications of this concept, some rather controversial, have been widely discussed, so that it appears timely to attempt an evaluation or survey of focal infection at this time.

The primary report of Billings comprised ten cases of chronic arthritis and six cases of subacute and chronic parenchymatous nephritis, the local infective focus in each instance being located in infected faucial tonsils, which when completely enucleated brought about a favorable therapeutic result.

A second article,² published in 1913, presented a study of seventy patients with arthritis deformans and confirmed the principles announced in the first article. It was found that the focal disease was usually located in the head and was most frequently a chronic streptococcal infection of the faucial tonsils. In this study arthritis deformans was regarded as an infectious clinical entity, manifesting chronic peri-arthritis, synovitis, proliferative and degenerative osteo-arthritis, chronic myositis with contraction of muscles and perineuritis or neuritis, as well as the usual coincident but secondary malnutrition and faulty metabolism.

In a paper read before the Section on Practice of Medicine in 1914 Billings³ discussed the broader application of focal infection in the etiology of general disease, considering it a chief factor in its etiologic relation to acute rheumatism, chronic deforming arthritis, gonorrheal arthritis, malignant endocarditis, myositis, myocarditis, septicemia of various bacterial types, tuberculous nephritis, visceral degeneration, certain infectious types of thyroiditis, acute and chronic pancreatitis, peptic ulcer, duodenal ulcer and cholecystitis.

The Lane medical lectures⁴ on the subject of focal infection were delivered in San Francisco in 1915. Billings defined the focus of infection as "a circumscribed area of tissue infected with pathogenic microorganisms" and said that the term focal infection implied

(1) that such a focus or lesion of infection existed, (2) that the infection was of bacterial nature and (3) that as such it was capable of dissemination resulting in systemic infection or infection of other contiguous or noncontiguous parts. This focus of infection might be located anywhere in the body and was usually in the head in the form of an alveolar abscess, a deep tonsillar or peritonsillar abscess or chronic sinusitis. Cholecystitis, acute and chronic appendicitis, a submucous or subcutaneous abscess anywhere, salpingitis, vesiculitis seminalis and prostatitis were regarded as further examples of local conditions. Over-repaired teeth could cause or prolong alveolar disease. A tonsillectomy might add a sealing scar to the infected tonsillar stump.

Billings contended that a new principle was not involved, because it had long been known that acute rheumatic infections, including arthritis and endocarditis, were frequently the result of primary infection in the faucial tonsils, that acute parenchymatous nephritis could result from the toxemia incident to diphtheria, that acute gonorrheal arthritis had its source in a focal infection in the urinary or genital tract and that acute severe localized infections in various parts of the body might give rise to disease in remote tissues. However, the importance from the standpoint of chronic, low grade, often symptomless infections in such regions, although emphasized repeatedly by good clinical observers, was not recognized until Billings and his co-workers recorded their clinical observations and correlated experimental studies on animals.

Many of the statements made in the first article regarding the concept of focal infection were destined to constitute definite arguments against subsequent criticism. For example, the experimental fact was recognized that a streptococcus from any source might produce acute articular lesions in inoculated animals, especially rabbits; that bacterial specificity was not established, and that general hygienic treatment was necessary for all classes of patients treated, this general treatment often having a good deal to do with the favorable outcome of the systemic disease.

It was definitely stated that the purpose was not to advocate unnecessary surgical procedure but to show that if focal disease existed it might produce acute disease or chronic degenerative changes in any organ of the body and should be radically eliminated and, finally, to call attention to a source of general disease which, while recognized by a few, was entirely ignored by the many.

Dr. Billings was fortunate in having available a large medical service and trained laboratory co-workers such as Drs. D. J. Davis, Leila Jackson, H. K. Nicoll and E. C. Rosenow. The last named became in a large measure the laboratory exponent of Billings, and his extensive investigation on the streptococcus and focal infection expressed the thoughts of his chief and at all times had his fullest endorsement.

The tissues and exudates of the different foci yielded various pathogenic bacteria, of which streptococci, pneumococci and staphylococci were most commonly found.

Gonococci were detected in infected fallopian tubes, seminal vesicles and related organs, and tubercle bacilli occasionally in tonsillar and peritonsillar tissues.

Organisms of the streptococcus group obtained from foci showed in many instances a pathologic specificity for certain tissues when injected into rabbits or other animals. The brilliant work of Rosenow⁵ in demon-

Read before the Section on Practice of Medicine at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 15, 1938.

1. Billings, Frank: Chronic Focal Infections and Their Etiological Relations to Arthritis and Nephritis, *Arch. Int. Med.* 9: 484 (April) 1912.

2. Billings, Frank: Chronic Focal Infection as a Causative Factor in Chronic Arthritis, *J. A. M. A.* 61: 819 (Sept. 13) 1913.

3. Billings, Frank: Focal Infection, *J. A. M. A.* 63: 899 (Sept. 12) 1914.

4. Billings, Frank: The Lane Medical Lectures, New York, D. Appleton & Co., 1915.

5. Rosenow, E. C.: *J. Infect. Dis.* 14: 1, 1914.

strating the transmutability of the micro-organisms of the streptococcus-pneumococcus group permitted at the time a better understanding of the changing pathogenicity of these bacteria. It was generally accepted that transmutation of a strain of this group could occur in the focus of infection, the oxygen supply of the tissues about the focus being an important factor in the transmutation.

These interesting experiments, carried on mainly by Rosenow, attempted to prove that strains obtained from patients with chronic arthritis, rheumatic fever with endocarditis and pericarditis, myositis, peptic ulcer (surgically excised), cholecystitis (surgically treated) and chronic infectious endocarditis (proved by blood culture) when injected resulted in the production of the respective lesions in the experimental animal.

It was on the basis of such experimental results that Rosenow⁶ introduced the term elective localization with special application to streptococci and started a controversial discussion, particularly among bacteriologists and immunologists, that continues to this day.

EXPERIMENTAL INVESTIGATIONS

For the next ten or fifteen years the interest in focal infection was largely concerned with experimental investigations pertaining to selective tissue affinity and elective localization either separately or in connection with special clinical observations. To a large extent the subsequent publications were either confirmatory or critical of the concept of focal infection advanced by Billings and the results of bacteriologic investigations reported by Rosenow and his associates.

The unusual results obtained by Rosenow were evidently due to the use of special culture methods devised by him for excised tissues, blood and other fluids, in which due regard was given to the question of oxygen pressure, particularly in primary cultures. Rosenow was able to obtain positive cultures frequently, while cultures made in the usual way remained sterile. For example, *Streptococcus viridans* was cultured in cases of chronic infectious endocarditis, while the usual cultures suggested the "bacteria-free" stage of Libman incident to this disease.

The relation of selective affinity for certain tissues formed the basis of elective localization of many of the pathogenic bacteria concerned with focal infection. This was conceived to be due to the circumstance that the conditions for growth are more favorable in some tissues than in others.

Following Rosenow's numerous publications on elective localization a mass of experimental work developed, of which only a limited number of instances can be cited at this time.

The work of Rosenow was confirmed in detail by Russell L. Haden,⁷ who followed closely certain fundamental technical details insisted on by Rosenow. The contribution of Haden was concerned primarily with the study of kidney lesions developing in rabbits as a result of the intravenous injection of bacteria, usually streptococci, recovered from patients with periapical dental infection. His report included also six cases of pyelonephritis studied to determine whether the condition from which the patient suffered could be reproduced in animals with the bacteria isolated from foci of chronic infection.

The material in every case was cultured in deep tubes of dextrose brain broth and dextrose brain broth agar mediums, in which the organisms found in chronic foci grew luxuriantly and also retained their elective affinity. The organisms recovered from patients with periapical infection were usually nonhemolytic streptococci. The animals were inoculated intravenously with 5 cc. of the twenty-four hour brain broth culture and killed in from three to six days. Four hundred and sixteen rabbits were inoculated and examined post mortem. Of this number 166, or 40 per cent, showed gross lesions of the kidney. The lesions encountered were cortical abscesses, pyelonephritis, acute hemorrhagic nephritis and subacute parenchymatous nephritis. By far the most common type of lesion was pyelonephritis manifested as edema, necrosis and abscess formation in the medulla of the kidney, usually extending well down to the tip of the papilla.

The frequency of kidney lesions occurring after intravenous injection showed clearly the great pathogenicity for kidney tissue of bacteria recovered from chronic foci. Also the type of lesion produced most commonly in animals corresponded to the lesion occurring most frequently in patients; namely, pyelonephritis.

Haden said that the most convincing proof of the relation of a focus to a disease was the reproduction in animals of the disease from which the patient suffered with the organisms recovered from a chronic focus in the patient. Additional proof was afforded by the effect of the removal of the focus on the clinical course of the disease. Six patients were studied in this connection, all having clinical symptoms of pyelonephritis. Twenty-eight rabbits were inoculated with cultures from teeth with periapical infection extracted from the six patients concerned, and in twenty-four, or 89 per cent, gross kidney lesions developed. In contrast to these results, only 40 per cent of all the animals inoculated showed kidney lesions.

The very much higher percentage of such lesions with cultures from patients with kidney disease showed clearly that the organisms in the infected foci had acquired some special affinity for kidney tissue. It was also most suggestive of a causal relation of the dental infection to the kidney disease. The improvement in the patients' condition following the removal of the chronic foci made the connection even more probable.

These results were confirmed by a second study of Haden,⁸ on the elective localization of bacteria in peptic ulcer. This study was on twelve patients with peptic ulcer. Streptococci were grown from the root tip of one or more teeth or from areas of infected bone in each case. In some cultures staphylococci were recovered with the streptococci. The streptococci were usually of the nonhemolytic type. All cultures were made in dextrose brain broth and dextrose brain agar, mediums which provide every degree of oxygen tension. Forty-five rabbits were inoculated intravenously with the broth cultures, the strain from each patient being injected into at least two rabbits. Twenty-four, or 53 per cent, of the animals showed at necropsy lesions in the stomach or duodenum or both. There were positive results in at least one animal for each patient.

During the period covered by these experiments, 55 other rabbits were similarly inoculated with cultures from the dental foci of 191 patients not known to be

6. Rosenow, E. C.: Elective Localization of Streptococci, J. A. M. A. 65:1687 (Nov. 13) 1915.

7. Haden, R. L.: Am. J. M. Sc. 169:407 (March) 1925.

8. Haden, R. L.: The Elective Localization of Bacteria in Peptic Ulcer, Arch. Int. Med. 35:457 (April) 1925.

suffering from peptic ulcer. Of these only forty, or 7 per cent, showed at necropsy lesions in the stomach and duodenum.

Another point advanced by Haden in favor of the causal relation of chronic focal infection to peptic ulcer and also of the theory of elective localization was the anatomic location of the gastric and duodenal lesions in the experimental animals. It is well recognized that gastric ulcer may occur in any part of the stomach but is much more frequent in the pyloric region. The experimental gastric lesions had a similar distribution. Clinically duodenal ulcer is always limited to the first third of the duodenum. In every animal but one in which a duodenal lesion was observed, the involvement was limited to the duodenal bulb.

These results furnished definite confirmatory proof of Rosenow's theory of elective localization and the infectious theory of peptic ulcer as well as of the theory that dental infection is an important factor in the causation of gastric and duodenal ulcer.

Holman⁹ published in 1928 a comprehensive critical review of focal infection and elective localization and arrived at some interesting conclusions. While admitting that focal infection is a principle of great importance in numerous disease conditions in man, he said that the factors determining the localization of bacteria which have entered the blood stream are those which alter the circulation, particularly those which modify the endothelium of the capillaries and thereby affect the nutrition of the cells of the tissues concerned. He claimed that the specificity of the bacteria involved had not been proved and that the evidence favoring the theory of elective localization was still open to misinterpretation. It was recognized that a certain general bacterial adaptation to environment is accepted by every one but that the factors on the side of the host are more variable and therefore far more important. The final comment was rather significant and somewhat contradictory: "What Rosenow and all the other investigators of the problem have definitely demonstrated is that streptococci do localize in various organs and tissues and can produce lesions at least sufficiently suggestive of those found in man so that their potential danger in infected foci cannot be neglected."

One of the most carefully controlled experimental investigations supporting the concept of focal infection and elective localization was published by Noble W. Jones and S. J. Newsom¹⁰ in 1932 and comprised the results of an interesting study of "experimentally produced focal (dental) infection in relation to cardiac structure." This was the first report on record of an experimentally controlled attempt to correlate the effect of focal infection with cardiac hypertrophy or to determine myocardial response to toxic injury and infection under stress and strain.

The problems discussed were (1) the relationship, if any, between experimentally produced focal (dental) infection and cardiac hypertrophy in dogs, (2) the relative effects of exercise on the hearts of infected and noninfected dogs, (3) the reliability of the various means of expressing cardiac hypertrophy and (4) other pathologic changes, cardiac and extracardiac, found in the experimental animals.

In the experiments twelve dogs had the distal half of a tooth removed. After the pulp was removed and the

cavity dried it was filled with a culture of streptococci isolated from a patient with chronic hyperplastic sinusitis; the pulp point was put in place and covered with cotton and dental cement and the tooth permanently filled with silver amalgam. Twelve dogs were selected as a control group and subjected to the same care and treatment but were not inoculated. In addition, seven normal dogs of the same age and weight were secured after death; the free hearts were weighed and kept for comparative study.

The inoculated and control dogs were subjected alike to daily exercise in which the stress and strain was carried to the point of exhaustion. The results indicated that the inoculated dogs showed more fatigue than the noninoculated dogs during the period of exercise. They lost weight more rapidly and the average duration of life was shorter. These experiments furnished, therefore, considerable clinical evidence that the inoculated dogs were made chronically ill by reason of their dental infection. There was also a certain suggestive similarity in clinical course and pathologic changes between the inoculated dogs and human beings suffering from those myocardial changes that are believed to follow at times in the wake of chronic dental and chronic sinus infection.

The results were summarized as follows: 1. Dental abscesses were demonstrated in all inoculated dogs. 2. The hearts of the inoculated dogs all showed very small vegetative or verrucose mitral and/or aortic endocarditic lesions, patchy parenchymatous degeneration, nuclear changes, increase in the diameter of the muscle cells and slight round cell infiltration. 3. A positive relationship between experimentally produced focal dental infection and cardiac hypertrophy as measured by diameters of muscle cells was noted. 4. Stress and strain in the absence of focal infection did not affect the gross or the microscopic characteristics of the heart.

Such results so definitely controlled must be regarded as distinctly suggestive of selective tissue affinity and elective localization.

Within recent months an interesting clinical and experimental study of rheumatoid arthritis was presented by Cecil and Angevine,¹¹ with special reference to the incidence of focal infection. The study was based on an analysis of 200 cases of typical rheumatoid arthritis from the records of the private practice of Dr. Cecil. The sedimentation rate was accelerated in 93 per cent of the cases. The agglutination reaction with a strain of hemolytic streptococcus was strongly positive in 65 per cent. The experimental studies included the intravenous injection in small doses of a hemolytic strain of streptococci (2 cc.) which produced arthritis in about 85 per cent of the injected animals.

Using the same organism, these workers attempted to create foci in rabbits at various selected sites, such as the gums, sinuses, male genitalia, eyes, pleural and peritoneal cavities, joints, skin, uterus, fallopian tubes, renal pelvis and gallbladder. Arthritis was produced in only 11 per cent of 100 rabbits inoculated otherwise than intravenously, and to accomplish this end it was necessary to use large doses of a suitable strain of streptococcus as well as a most susceptible animal. It was concluded that as experimental foci the gums are a particularly favorable site for the absorption of bacteria and that it is difficult to establish a chronic persistent focus of infection in rabbits.

9. Holman, W. L.: *Arch. Path. & Lab. Med.* 5: 68-136 (Jan.) 1928.
10. Jones, N. W., and Newsom, S. J.: *Experimentally Produced Focal (Dental) Infection in Relation to Cardiac Structure*, *Arch. Path.* 13: 392-414 (March) 1932.

11. Cecil, R. L., and Angevine, D. M.: Paper read before the American College of Physicians, April 4, 1938, at New York; to be published.

To the two investigators concerned these results seemed to indicate that chronic focal infection plays a comparatively unimportant part in typical rheumatoid arthritis. That the experimental foci produced in various tissues of rabbits can be regarded as analogous to conditions in the human organism is perhaps open to discussion.

About five years ago Rosenow and Jensen¹² announced the interesting fact that there is a close parallelism between elective localization and cataphoretic time and velocity of streptococci and that the respective serums have specific potential lowering effects on these streptococci. Rosenow¹³ stated that the method of determining cataphoretic velocity has yielded results of etiologic importance and that if this method is properly applied it is no longer necessary to inject cultures from atria of infection intravenously into animals and to make cultures from their joints in order to be certain that the streptococcus isolated is causative or has characteristic infecting and antigenic powers. Determination of the cataphoretic velocity is usually sufficient.

Any impartial view of the mass of experimental and clinical studies that have been recorded must recognize that this evidence is supportive of the fundamental conception of an infectious process, in that many pathogenic bacteria possess a predilection for certain tissues.

The pneumococcus is prone to localize in the lungs, and *Bacillus typhosus* has a definite predilection for the lymphoid elements of the gastrointestinal tract. The typhoid carrier offers a striking example of the chronic localized focus.

On the other hand, it is well established that organisms of the streptococcus group may invade almost any tissue of the human body and give rise to a great variety of pathologic changes. This was recognized by Forssner¹⁴ as early as 1902, although the great importance of this elective tissue affinity was not recognized until many years later.

The results of the experiments which have been cited emphasize the importance of foci of infection as places in which bacteria may grow and acquire elective pathogenic properties which determine their mode of action and distribution after their entrance into the blood stream.

Within the inner circles of the bacteriologist and the immunologist, specific tissue affinity and elective localization are still subjects of controversy, yet the tenets of both sciences offer definite confirmation regarding this fundamental concept of focal infection, and perchance it is safe to assume that the "Rosenow heresy" may yet become the medical guide of the future.

CLINICAL OBSERVATIONS

Concurrently with experimental investigations, critical clinical observations in great numbers have been reported within the quarter century, and any impartial reviewer must admit that they lend the fullest support to the dictum spoken by Billings in 1932, twenty years after his original contribution: "Focal infection as an etiologic factor of general disease is now an established pathological principle."

The significant relationship of oral conditions to conditions elsewhere in the body is now widely recognized,

for which fact no doubt the advances in the domain of dental medicine are in large measure responsible.

Focal infection implicating the nervous system has been emphasized by Foster Kennedy¹⁵ and other neurologists, who point to the frequent occurrence of referred pain (myositic) with tonsillitis, the more limited incidence of transverse myelitis, the occurrence of peripheral neuritis and of neuritis of the cauda equina caused by various local infective foci, as well as the involvement of the nervous system in diphtheria.

MacCallan¹⁶ of London has directed attention to the relation to ocular disease of chronic focal sepsis occurring in chronic inflammations of the intestinal tract, the gallbladder, the accessory sinuses, the prostate, urethra and the pelvic organs of the female, elimination of the infective focus producing a cure or improvement in the condition.

According to Ayers and Anderson¹⁷ focal infection plays a dual role in dermatology, in that cutaneous disorders may act as foci of systemic infection and, *vice versa*, focal infection may be an important etiologic factor in diseases of the skin.

Harry Weiss¹⁸ has recently analyzed 364 cases of subacute bacterial endocarditis with particular attention to antecedent history and the manner of onset. The chief feature noted was the frequency with which the onset was associated with an immediately preceding acute infection of the upper part of the respiratory tract, tonsillitis or influenza. Another significant fact was the frequency with which a preexisting pathologic condition of the endocardium was demonstrable. The frequency of antecedent cardiac disease, usually rheumatic but sometimes atherosclerotic, syphilitic or congenital, indicated that the infection required a previously diseased or abnormal endocardium on which to implant itself. The history of a tonsillectomy or extraction of a tooth often closely antedated the onset of symptoms. Infections of the genito-urinary tract, otitis media and wound infections were further sources of portals of entry.

William Hunter of London as early as 1910 directed attention to the causal relation of oral sepsis to secondary or hypochromic anemia. Murphy¹⁹ has recently emphasized again the frequency of pyorrhea and dental abscesses in the early history of pernicious anemia. That such conditions have etiologic significance in the macrocytic anemias is being generally recognized. Chronic arthritis has always been closely associated with the concept of focal infection. While gonorrhea and arthritis forms a classic demonstration and in many cases of chronic arthritis focal or other infections are accepted as the cause, there is still a strong belief that in all cases the disease is not due to this agency alone.

It has been suggested by Pemberton²⁰ and others that the pathologic changes of arthritis and the rheumatoid syndrome depend on disturbances in the blood supply of the parts involved, particularly the fine capillaries. With this opinion Billings²¹ expressed his agreement shortly before his death in 1932 and recalled the statement in his early publications as to the pro-

15. Kennedy, Foster: *Am. J. M. Sc.* 185: 305-314 (March) 1931.
16. MacCallan, A. F.: *Ocular Disease and Focal Sepsis*, Arch. Ophth. 3: 673-683 (June) 1930.

17. Ayers, Samuel, and Anderson, N. P.: *Focal Infection in Dermatology*, Arch. Dermat. & Syph. 34: 421-431 (Sept.) 1936.

18. Weiss, Harry: *Relation of Portals of Entry to Subacute Bacterial Endocarditis*, Arch. Int. Med. 54: 710-719 (Nov.) 1934.

19. Murphy, W. P.: *Lancet* 1: 1451-1454 (June 27) 1936.

20. Pemberton, Ralph; Cajori, F. A., and Crouter, C. Y.: *The Etiology of Focal Infection and the Pathology of Arthritis*, J. A. M. A. 6: 1793-1798 (Dec. 5) 1925; 87: 2148-2151 (Dec. 25) 1926.

21. Billings, Frank: *Bull. New York Acad. Med.* 6: 759 (Dec.) 1930.

12. Rosenow, E. C., and Jensen, L. B.: *J. Infect. Dis.* 52: 167-184 (March-April) 1933.

13. Rosenow, E. C.: *Cataphoretic Velocity of Streptococci as Isolated in Studies of Arthritis*, Arch. Int. Med. 51: 327 (March) 1933.

14. Forssner, G.: *Nord. med. Ark.*, 1902, 3. f., ii afd. 2, No. 18, p. 1.

ability that hematogenous infection by bacterial emboli or their toxins is a large factor in the diminution of the circulation of blood, especially in the smaller blood vessels.

According to Irons²² the current trend of thought concerning arthritis recognizes that the concept of chronic arthritis as a general disease rather than as a disease of the joints alone is steadily gaining ground. It is generally conceded that there are many initiating and contributing causes of chronic arthritis. These include infection, trauma, age, heredity, disturbances of the vascular supply or of the general and local nutrition, and metabolic and glandular dysfunction. No single cause or condition is common to all cases of arthritis.

In future etiologic studies the classification of chronic arthritis into two great types, the atrophic (rheumatoid) and the hypertrophic (osteo) arthritis, will be extremely serviceable, and the exact relationship of focal infection to arthritis, particularly the atrophic or rheumatoid type, will be more clearly understood.

COMMENT AND SUMMARY

In any attempted survey or evaluation of the present status of focal infection it must be evident that such infection has come to occupy a very important place in the activities of medical and surgical practice and of the various specialties.

It has been remarked that it has greatly enhanced the opportunities of certain specialists.

With increasing knowledge of the various phases of the problem a more conservative attitude has developed with reference to hasty diagnostic conclusions and radical removal of the suspected foci of infection, with added emphasis on a more careful analysis of all possible etiologic factors connected with the condition concerned. There is a growing conviction that treatment should be based on the results of an accurate and complete diagnosis, the physician remembering that it is the patient with a focal infection who requires treatment and not the focal infection alone.

It is well to recall the discussion of Billings²³ before the Section on Practice of Medicine in 1920, in which he said: "Focal infection as a cause of disease has come to stay. But, like every other principle in medicine, it has its limitations." He said further:

Much of the fallacy and failure in the treatment or management of patients who suffer from what may be proved to be focal infection is due to the fact that the surgeon or physician in charge removes a focus, which may be the right one, and then neglects any further management of his patient. And, if, what I have just said is true, then the removal of the focus has not disturbed the organisms already in the tissues of the body. If you have removed the true focus, you have simply prevented the invasion of the tissues by additional organisms from the primary focus.

In spite of the critical attitude maintained in certain quarters regarding the continued acceptance of the concept of focal infection, it should be acknowledged that the efforts that have been proposed to detect and then to obliterate all forms of focal infection in the mouth and throat as well as elsewhere in the body for preventive as well as for curative purposes, besides being in accord with sound reasoning from general principles, has received the support of strong experimental evidence.

The constant correlation of experimental investigation with careful clinical observations has distinctly influenced diagnostic procedure for both the medical and the surgical specialist as well as for the general practitioner.

With a fuller appreciation of the limitations of special consultant service, the responsibility of the general internist or diagnostician has assumed a much greater importance. The correct interpretation of all the factors concerned with the causal relationship of focal infection to systemic disease requires diagnostic skill and judgment of a high order.

Perhaps the real contribution of the concept of focal infection is a fuller appreciation of the higher professional attributes involved in careful diagnostic conclusions and more complete treatment of patients, which are well exemplified in the life and service of Dr. Frank Billings.

Bankers Trust Building.

FUNCTIONAL OR SOCIOLOGIC DISORDERS OF THE COLON

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Persons who have a functional disorder of the colon which may have been excited by social conditions describe symptoms which they believe arise in the colon, but when the colon is examined it is found to be free of physical changes which are indicative of organic disease. The disorder is manifested by irregularities of defecation and apparent alteration in the absorptive and secretory functions of the colon. It frequently is associated with abdominal discomfort, pain and often with mucus in the feces and subjective abdominal distention. Variations in these symptoms are the rule. However, the patient will rarely admit of periods without some "suffering." Changes in symptoms may be related to changes in the quantities of mucus present in the feces. Alternating periods of constipation and diarrhea are not uncommon, but the outstanding symptom usually is either diarrhea or a constipation.

Our object in this paper is to present what we think initiates a large part of the functional disorders of the colon during adult life and to tell how they may best be treated. If the exciting etiologic factor is intellectual and emotional weaknesses, one must show the patient his personal responsibility instead of resorting to the administration of placebos. Likewise, if the symptoms are due to unsuitable moral and religious tendencies or are the result of erroneous interpretations of defecitiveness, disease or supposed misconduct of the colon, recovery may be attained only through mutual responsibility. The patient's confidence from the beginning is, therefore, of utmost importance. A patient may refer to the fact that his father and mother possessed beliefs or traits similar to his own and that he cannot be different. It is not true that what man is was fore-ordained when he got his supply of genes in the germ cells. Every person has many sets of possible heredi-

22. Irons, E. E.: Presidential address, Proceedings of the American Association of Rheumatic Disease, June 10, 1935, p. 5.

23. Billings, Frank, in discussion on Fontaine, B. W.: A Clinical Study of the End-Results of Some Focal Infections, J. A. M. A. 74: 1631-1632 (June 12) 1920.

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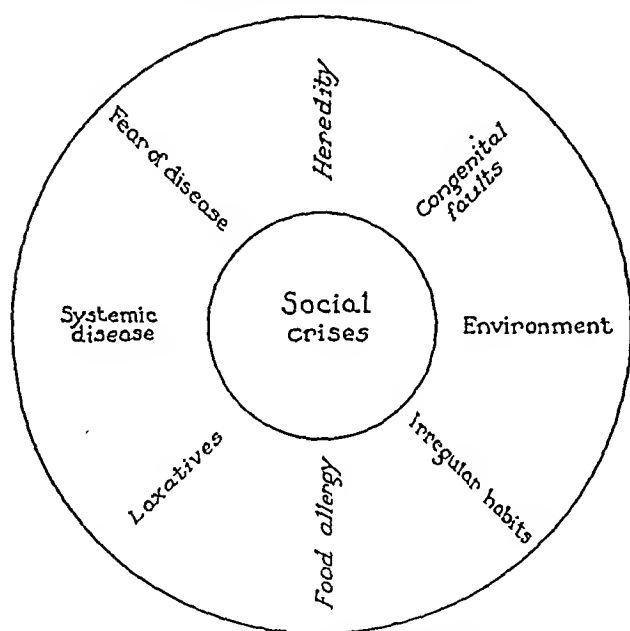
tary characters. The conditions under which he develops determine which set of characters he shall bring forth. It is the conditions which originated the belief that he is foredoomed that physicians may be able to modify. At some recent or remote time in the past history it usually will be found that insufficient rest, fear, anxiety or failure of relaxation has been operative. The beginning of the first serious disturbance of habit is often occasioned by sickness, accident, unexpected loss of money, property or job, or death of a member of the family, betrayal of confidence by a friend, migration, or change of party, church or occupation. The onset of a diarrhea or constipation at such a time is perplexing. This or that remedy is tried, and if no results are obtained the crises which originally initiated the insufficient rest and relaxation may be forgotten and the patient may become unadjusted socially on account of the colonic symptoms. He feels that the disease is organic in origin. Repetitions of crises may often occur, and the patient finally

anemia with the associated achlorhydria, and poisoning by lead or other heavy metals, exophthalmic goiter or Addison's disease all may be accompanied by intestinal symptoms which may be most difficult to evaluate and usually require careful study. In times, in cases of systemic disease, it is advisable to treat the patients as though they had a functional disorder of the colon until a definite diagnosis is made. One should not jump to a diagnostic conclusion and institute unnecessary or possibly harmful treatment. Fevers, infectious diseases, septicemic conditions, nutrition from any cause, pelvic and abdominal and deranged functions of the pancreas, liver and kidneys are at times accompanied by colonic symptoms to such a degree that the underlying disease is masked.

Suggestion may be the basis for initiating a study. The suggestion may be obtained from conversation with one who actually suffers from organic disease of the colon. A symptom resulting from a suggestion made during consultation with a too casual physician or surgeon, or obtained from a patient who has an organic disease of the colon, may be most difficult to evaluate. One must remember that no patient is immune unto himself. Whatever interrupts the smooth running of his personal affairs may be reflected by his symptoms.

Environment.—Environment exerts profound influence on all forms of life. Man has done his best to stabilize the physical factors of his environment. In doing this he has imposed on himself a most interesting competitive and machine-like routine of living by accounting for his time on time clocks, at bargain counters and paying his bills on the installment plan. As though this mechanical existence is not enough, he is haunted by the desires and anxieties of his family. By contrasting this environment with the sulky existence of primitive man, without the gains of his power, influence and worldly possessions by means of the machine, one may gain an idea of the ever changing conditions in which the human lives. Intrigue and politics are not physically disabilities. Environmental changes may be derogatory. The girl from the carefree life of the small town who is forced to earn her living away from home and live in cramped quarters with limited bathroom facilities is almost certain to be troubled with constipation. Environmental conditions create social crises which are important etiologic factors in functional disorders.

Fear of Disease.—The fear of disease within certain limits is an important ideal for an individual in a community. But when this fear grows big enough to interfere with daily life it may produce disability. Those who are fearful of disease of the colon are constantly tantalized by advertisements of remedies which prevent auto-intoxication and colitis. These advertisements may suggest unnecessary prophylactic measures and unhygienic and unphysiologic requirements of the patient. Any fears of the patient should be treated with the greatest of caution and sympathy by the physician. A jocular attitude toward a fearful patient will drive him into the hands of an apparently sympathetic person who may employ ill advised and ineffectual treatments which will result in the development of unmanageable fears and colonic disorders. An air of sympathy and a thorough examination are required as a beginning to convince the patient



Diagrammatic representation of etiology of sociologic diseases of the colon.

may become completely demoralized. All of this is important to the physician because intelligent management of the colonic disorders during a crisis will prevent many of the patients from becoming maladjusted and certainly will decrease the number of colonic invalids seen in the demoralized fraction of society.

ETIOLOGY

In order to facilitate description of the etiology of these disorders, the accompanying diagram has been arranged. The inner circle of the diagram should be considered as the hub of the etiology, and radiating from this hub, like the spokes of a wheel, are other factors which are exciting causes. Some such graphic arrangement aids greatly in a study and especially in obtaining a history and evaluating the symptoms, which are exceedingly important in the treatment of these disorders.

Systemic Disease.—The possibility of systemic disease must be considered in every case of functional disorder of the colon. Deficiency diseases such as pellagra and sprue must not be overlooked. Pernicious

does not have organic disease. In families in which disseminated polyposis or carcinoma of the colon or rectum, or ulcerative colitis, has occurred, a fear of these diseases is genuine. This fear is often precipitated by the presence of mucus in the feces. Mucus is normal but variable secretion of the colon and not a sign of disease.

The patients who suffer from a disorder of the colon which results from the fear of disease of the colon or elsewhere in the body may be classified in two groups. The first group comprises those who are intelligent and who have a good, sound basis for their fear, such as an unexplained diarrhea, following a recent pulmonary tuberculosis or time spent in a tropical climate. The patients in this group are temporarily unadjusted and will recover if proper advice is given by the physician. The second group includes patients whose judgment is fallacious. Their conception is that they have a disorder of the bowels; their complaints and their "case" are different from any they imagine that the physician has ever seen. They are worthless to themselves, miserable, arrogant, evasive and difficult, if not impossible to treat successfully.

Laxatives.—The use of laxatives is as old as the human race itself. A good laxative gave the early physicians a means of producing results which demonstrated to the patient the potency of their medicine. When the colon has been emptied with a laxative, it becomes filled with liquid feces and gas. If there is any tendency to irritability, the presence of the gas and fluid may produce discomfort. It is doubtful, however, whether the repeated use of laxatives by normal persons will produce anything more than a mild functional disorder of the colon which will subside as soon as the purgation is discontinued. The habitual user of purgatives punishes the colon because of erroneous ideas of its proper function.

No part of the etiology of functional disorders of the colon has received more attention than that of laxatives. The question may be justly asked whether the laxative habit precedes or follows the disorder. The continued and increasing use of drugs to produce defecation is so obviously injurious that it needs no elaboration to the physician.

One of the oldest and most popularized theories of the cause of functional disorders of the colon assumes that retained alimentary waste materials produce toxins, which in turn are absorbed by the intestine and thus poison the body. Scientific data which will either prove or disprove this theory are lacking. Indican in the urine has been assumed to be an index of "colonic stasis." Indican is a conjugated sulfate, indoxyl sulfuric acid. This fact alone would indicate that the possible toxic effects of indoxyl probably have been quickly and effectively neutralized by being conjugated with sulfuric acid.

Congenital Faults.—Congenital faults in the development of the colon conceivably could be of etiologic importance in a functional disorder. It, however has been the experience of all careful observers that congenital malformations do not produce symptoms that are as indefinite and as obscure as those often present in a functional disorder. If one began to theorize that a faulty development of the intestine or colon was etiologically important, objection to this theory could be raised on the basis that congenital malformations and variations are always present. What is more important is the fact that a congenital fault often could not be

proved to be a developmental defect but a hereditary pattern. We believe that variation in the length or position, or ptosis of the colon is compatible with a comfortable abdomen and bowel habits. We do not believe that the erect position of man produces digestive handicaps.

Allergy to Food.—Much research and thought have been directed toward solving the important problem of allergy to certain foods. Those who are too sympathetic toward the idea of food allergy vision an allergy to some food in every case of indefinite abdominal symptoms. Of the total number of patients who have these symptoms, relatively few will respond favorably to the so-called elimination diets or will respond positively to dermal tests with food extracts. Allergy, if considered on a sound scientific basis, follows certain definite clinical trends. If the patient is allergic, he should have symptoms which can be explained on the basis of spasm by smooth muscle, other manifestations of allergy should be present, a positive family history for allergy should be obtainable, the cutaneous tests for allergy should be positive, and eosinophilia should be present.

The results produced by an elimination diet have no objective controls. The physician is forced to interpret the subjective discourses of a patient whose disorder is characterized by vague descriptions and often by fabrications and evasiveness. One tries to evaluate the effects of foods on symptoms which are often figments of the imagination, and above all sitophobia may be an important symptom. Where sitophobia is present, good results will be obtained with the initial diet, but the further addition of foods inevitably produces distress and suffering. Often so-called food allergies are produced by eating quickly or, in other words, by "bolting food" at irregular hours. Such abuses often promote physical and mental abuses and excuses for excessive use of tobacco, coffee and alcohol.

Irregular Habits.—Some of the irregular habits conducive to the production of functional disorders of the colon have been mentioned. The largely artificial environment created by what we call our present civilization makes no allowance for the creation of regular bowel habits except the provision of toilet seats which are too high for a comfortable natural defecation. A certain degree of relaxation during work, sleep and periods of full relaxation, such as obtained while on a suitable vacation, are necessary and, if obtained, the question of bowel habits would not be known except during the unavoidable social crises during a lifetime. Irregularity prevents relaxation and annuls sensations. When there is an increased number of bowel movements during the day, regular habits for meals, without extreme temperatures of foods and beverages, may be beneficial. In cases in which there is an increased gastrocolic reflex, a change in the hour of the morning meal, as well as slowly eating of foods at about body temperature, is imperative. Many vicious habits of eating, sleeping, defecation and work are absolutely unrecognized by the patient. These can be ascertained only by taking a detailed clinical history.

Heredity.—Barring accident, when one is born one is endowed with potential capabilities, mentally and physically. These capabilities are mixtures of those possessed by one's progenitors. One's mental habits, conduct, hours of sleep, foods and drinks are intimately associated with one's environment, but they may be closely related to physical endowments of heredity. Of

the physical endowments of heredity, that of stature seems to be of the greatest importance, for a sturdy blond rarely has a sociologic disorder of the colon; typically it affects the tall, slender brunet. At birth one either possesses the type of nervous system of the stoic or that of the "nervous" irritable person. Environment with its harmful or beneficial influences yields what the physician has to work with. One cannot avoid the impression that a proper physical and social environment would prevent the physician from seeing many of these unfortunate persons.

SYMPTOMS AND PHYSICAL SIGNS

The clinical history of a functional disorder of the colon may subjectively reveal the presence of every known symptom which can arise from organic disease of the colon. The bowel habits range from profound constipation to watery diarrhea. Often these symptoms alternate from a watery diarrhea to a stubborn constipation.

The diarrheal phase is the most distressing. It is likely to cause the greatest inconvenience after breakfast. Secretion of mucus, which is one of the principal functions of the colon, may be deranged so that small quantities are passed with each bowel movement, or an entire bowel movement may consist of mucus. The patient often is led to believe that worms have been passed. Mucus is frequently white and stringy and presents pseudomovements as a result of drying.

In eliciting the history, there are certain facts to be ascertained. Organic disease is likely to be ushered in with fever, loss of weight and perhaps blood in the stool. A functional disorder arises during or following the stress and strain of a social crisis. When the symptoms are intermittent, exacerbations come during subsequent crises. In some cases, when the environment has not changed the symptoms become constant. When the patients live in normal environments, a social crisis produces a permanent maladjustment and thus causes constant symptoms. The symptoms of organic disease are likely to be progressive or cease to exist.

The results of general physical examination in any phase of this disorder are not characteristic. Many normal persons have a palpable cecum, ascending colon or sigmoid colon. Abdominal tenderness may be accompanied by hypersensitiveness to pressure throughout the body. Often there are hyperactive reflexes, a tendency to fabrication, evasiveness, arrogance, irritability, and fixed and usually erroneous ideas concerning the illness. It is important to remember that organic disease may coexist or be superimposed on a functional disorder of the colon.

DIAGNOSIS

The diagnosis of a functional disorder of the colon depends on the following criteria: 1. Three specimens of fresh liquid feces obtained, if necessary, by the administration of saline purgatives should not contain ova or parasites. 2. Proctoscopic and sigmoidoscopic examination should reveal a normal mucosa and normal mobility of the bowel. 3. Roentgenologic examination of the colon and terminal portion of the ileum by means of an opaque enema, after adequate preparation, should not disclose any abnormality (if the ileocecal segment of the bowel is not visualized it may be necessary to administer the opaque medium orally). 4. Free hydrochloric acid should be present in the gastric contents after administration of a test meal.

5. The basal metabolic rate should be within normal limits. The last two of these examinations are not necessarily routine. The judgment of the examiner must be relied on in determining the necessity for further examinations to rule out endocrine disturbances, just as for the necessity of other special tests, such as cutaneous tests for possible allergy, and examination of the blood and urine for detection of possible poisoning with heavy metals. That is, the diagnosis is made in the process of elimination.

TREATMENT

At this time suggestions on therapy will be specifically applicable to young and middle-aged adults. The peusis by drugs resolves itself into the treatment of diarrhea and constipation.

In phases of constipation, the only laxative which should be used is one that acts by forming a nonirritating bulk. Crude or flake agar in doses of from 1 to 4 ounces (30 to 120 Gm.) administered in cereal or milk is the most reliable.

The success of treatment of diarrhea depends on acquainting the patient with his reactions and the effect of a social crisis. He should be made to understand that the colonic discomforts are reflex phenomena and not the result of an organic disease. One should prescribe few drugs during the crisis, but the patient should be made to rest and relax and an attempt should be made to allay the anxiety. These measures are accomplished by a regimen aimed toward physical rehabilitation. In brief, at the onset of the disorder a simple outline which aims at regularity of meals, bowel movements and exercise is the treatment of choice. If the disorder is chronic or if the patient is socially maladjusted, treatment should not be started until the patient has been convinced that all effort to discover latent disease have been exhausted. Fixed ideas concerning the illness, and arrogance and evasiveness are often a part of the disorder when it has become chronic. Therapeutic success is directly proportional to the degree of these symptoms, which may be measured as indexes of the patient's ability to make successful readjustments.

The treatment of the symptom diarrhea consists in the administration of drugs by mouth or by rectum and the control of the intake of food and fluids. The drug which may be administered orally may be considered under several headings. The best drugs for lessening bowel movements are the alkaloids of opium. It is rarely justifiable to administer these drugs. Of opiates, tincture of opium is the best. It should be administered three or four times daily in doses of 5 minims (0.3 cc.). However, some patients prefer camphorated tincture of opium, which should be administered in doses of 1 drachm (4 cc.). The tannic acid series and the mucilaginous herbs are the active substances in all folklore and Indian remedies for intestinal disorders. Lime water, lead acetate, bismuth subnitrate and atropine have enjoyed unwarranted popularity. Reasonable quantities of any known drug cannot be expected to pass through the buffers of the intestine and act effectively in the colon. Inert clays, ground to colloidal proportions, might be effective if sufficiently large doses could be given. An effective dose of the "powders" always absorbs sufficient material from the twenty feet of small intestine before reaching the colon to render it inactive. However, powders such as bismuth subnitrate (in teaspoonful doses) may have definite psychic value. Before attributing therapeutic

value to a drug in diarrhea, it must be recalled that this condition usually subsides spontaneously. In cases in which it is associated with achlorhydria, dilute hydrochloric acid in doses of from one-half to 1 drachm (2 to 4 cc.) should be administered by mouth (sipped through a glass tube). Tincture of iodine in doses of 10 minims (0.65 cc.) in a full glass of water may be effective. Systemic sedatives are often required and may be most valuable. Of these, either phenobarbital or the elixir of triple bromides is the safest. One-half grain (0.032 Gm.) of phenobarbital may be given three or four times daily. Fifteen grains of bromides may be given three or four times daily.

Except when they have severe diarrhea, patients should be placed on a wholesome normal dietary regimen. The human digestive system is structurally unfitted for the digestion of cellulose. If indigestible residue, such as wheat bran, is ingested, it will produce bowel movements for a short time until the colon becomes adjusted to the new stimulus. If the dietary and therapeutic regimens are changed too frequently the colon is required to change its habits. This change in habit is opposed to ideal treatment. A basic principle in ideal treatment is a regularity of habits, with periods of rest and relaxation which are strictly enforced. To this regimen should be added harmless remedies and other measures that are required to satisfy the patient.

The regular intake of water is often beneficial. These patients should receive enough water so that after the morning specimen of urine is voided the urine is practically without color the rest of the day. There is no reason to restrict the intake of salt. In the presence of severe diarrhea, the patient may become dehydrated and it may be imperative to maintain an increased intake of salt and water. If it is impossible to maintain normal urinary excretion by the oral administration of water and physiologic solution of sodium chloride, the deficit of water and salt should be made up by intravenous injections of physiologic solution of sodium chloride. During acute diarrhea, abdominal cramps often occur. The frequent passage of watery stools may irritate the anus, which becomes sore and painful. The application of heat to the abdomen and perineum is desirable. Rectal suppositories are usually not effective because they are expelled immediately. If the appetite is capricious, between-meal feeding may aid in maintaining sufficient caloric intake. In this state of hyperirritability of the intestine the diarrhea may stop abruptly. Rectal instillation of 2 or 3 ounces (from 60 to 90 cc.) of warm olive oil twice daily and the administration of sufficient tincture of belladonna to produce pharmacologic effects, which are evidenced by dryness of mouth and throat, may aid in restoring intestinal function.

In a few cases the history will reveal that during a phase of constipation repeated purgation, daily enemas or colonic irrigations had been prescribed. At first such a regimen had produced considerable relief, but later the abdominal pain and constipation had become more obstinate and finally an operation had been performed. At the time of the operation only chronic appendicitis or adhesions had been found. After the operation there had not been any discomfort for a short time and then there had been a recurrence of the abdominal pain and constipation. Such a history is very perplexing because the abdomen has been opened one or more times and there is the possibility of a mechanical ileus. Such a

case requires most serious consideration because the syndrome of spastic ileus usually should not be treated surgically.

A spastic ileus is generally a benign affliction. It usually affects those who have functional colonic disorders. Patients have died of a spastic ileus which had been treated with and without operation. There is no way to determine what the outcome would have been in any one case if another procedure had been resorted to. The difficulty lies in the fact that the clinical symptoms of mechanical and spastic ileus are the same. In both cases the illness may be acute or chronic, and the mischief may be situated in any segment of the intestine. There are two important differential points in making a clinical diagnosis. The first is the condition of the patient. In spastic ileus the general condition of the patient remains good for a long time, while in mechanical obstruction the patient may fail rapidly. A spastic ileus is likely to subside spontaneously in a short time. The second point is the duration of symptoms. Spastic ileus most commonly affects patients who have had a functional disorder of the colon. In our experience, spastic ileus most frequently affects patients who have been energetically treated by enemas, by strong purgatives and often by colonic irrigations. The previous history and treatment are not safe criteria for making an immediate decision as to the correct therapy. Such criteria can serve only as secondary aids in deciding on the proper course to pursue. It also is recognized that if it always were possible to make a diagnosis of spastic ileus the treatment should not be the same. Spastic ileus may be initiated in otherwise normal persons by foreign bodies, worms, undigested food, hemorrhage, circulatory disturbances, and reflexly by diseases of the central nervous system and perhaps at times by other indefinite causes. Treatment of these conditions cannot be outlined; it falls into the field of emergency medical treatment and, as long as the patient's general condition is good, one should not resort to operation.

Surgical treatment of the functional disorders of the colon, as an adjunct to rational therapy, is definitely contraindicated. When operation is performed in the absence of organic disease, it denotes an error in surgical judgment. There is much misconception relative to the importance of ptosis as an important factor in these disorders, and surgical procedures have not infrequently been advocated and performed with varying degrees of success, depending rather on the honesty of the surgeon than on the necessity of the procedure. Success of operation, in other words, has not been noteworthy.

A patient with a functional disorder of the colon may require surgical intervention for other abdominal disease, and fine differential diagnostic judgment is often required in such cases. When it is necessary to operate under these circumstances, it is important to make sure that the patient understands that the proposed operation is not intended to alleviate those abdominal symptoms referable to the functional disease. Surgical advice, therefore, in functional diseases of the colon consists, for the most part, of advice against surgical intervention.

SUMMARY

It is evident that the cure of these functional disorders is not to be sought merely in certain dietary rearrangements but in attempts to control scientifically the adverse social conditions. This is not always possi-

ble because many patients, from the standpoint of heredity, are incapable of meeting the exigencies of life and are therefore socially pathologic. In order to eliminate these disorders, the defects in education, government, religion, morality, philanthropy and even physical heredity have to be corrected. This ideal may be approached when there is a scientific understanding of the conditions necessary for normal social life. This ideal will never be attained by treating these patients for "colitis." It is only necessary to say in conclusion that the wisest measures should be directed toward the prevention of these disorders as well as toward the reclaiming of those who have already been caught in their meshes.

THE TREATMENT OF RHEUMATOID ARTHRITIS WITH LARGE DOSES OF VITAMIN D

A CRITICAL EVALUATION

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In 1935 Dreyer and Reed¹ reported that they had previously observed² marked clinical improvement in the rheumatoid arthritis of two patients during the time they were receiving massive doses of vitamin D for hay fever. This original report and other reports by the same authors³ have resulted in an increasing interest in the value of vitamin D in the treatment of rheumatoid arthritis as shown by subsequent reports.⁴

Knowing that generalized decalcification is a common and at times an early manifestation of rheumatoid arthritis, one might be led to suspect that the chance observation of Dreyer and his co-workers⁵ indicated that certain patients with rheumatoid arthritis suffer from some type of disease of calcium and phosphorus

deficiency. If such were the case, then this chance observation might be of etiologic as well as of therapeutic significance. However, detailed studies of the calcium and phosphorus metabolism of patients with rheumatoid arthritis have failed to reveal metabolic changes of sufficient degree to allow one to conclude that the generalized decalcification is secondary to a primary disturbance of calcium and phosphorus metabolism.⁶ This being true, one might conclude a priori that any improvement noted in patients following the administration of vitamin D was not the result of correcting a previously existing alteration of the calcium and phosphorus metabolism. An additional reason for doubting that such is not the *modus operandi* of massive doses of vitamin D is suggested by our failure to observe any material alteration in the course of the disease in patients receiving from 5,000 to 15,000 U. S. P. units of vitamin D daily for as long as from six to thirty months.⁷ This dose of vitamin D, although not adequate for the cure of all diseases of calcium and phosphorus deficiency, is sufficiently large to correct a good percentage of them.⁸

Irrespective of the aforementioned facts, Dreyer and Reed¹ reported improvement in twenty-five of thirty-four patients with rheumatoid arthritis treated with large doses of vitamin D, and others⁹ have reported equally encouraging results. Some reports¹⁰ have been less enthusiastic. Other workers¹¹ have stated that further trial with this form of therapy is necessary before any final conclusions are drawn concerning its efficacy. The results obtained by previous workers are briefly summarized in table 1.

METHOD OF STUDY

Because of the therapeutic and etiologic significance that might be attached to the foregoing reports concerning a chronic disease of unknown etiology, it was deemed necessary to evaluate as critically as possible the therapeutic effectiveness of massive doses of vitamin D in the treatment of patients with rheumatoid arthritis. Since rheumatoid arthritis is a chronic disease of years' duration, characterized by remissions and relapses of varying length and degree, the course of the disease may vary considerably from patient to patient. Therefore, in a study of this type, designed to determine the therapeutic effectiveness of a particular form of therapy, one must of necessity require that each person serve as his own control. Only in this way can one determine whether or not the therapy has altered the course of the disease. If this precaution is not taken, one will all too frequently conclude that the observed improvement is the result of the therapy employed, whereas it may represent nothing more than a natural fluctuation in the course of the disease. This manner of controlled study can best be accomplished by choosing only those patients whose clinical course has been known for months or years on a constant regimen prior to the institution of any so-called specific form of therapy. Equally important in this type of study is an adequate follow-up period on the same

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From the Medical Clinic of the Massachusetts General Hospital, the Department of Medicine, Harvard Medical School, and the Massachusetts Department of Public Health.

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4. These include: Livingston, S. K.: Vitamin D and Fever Therapy in Chronic Arthritis, *Arch. Phys. Therapy* 17: 704 (Nov.) 1936.

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Steck, I. E.; Deutsch, H.; Reed, C. I., and Struck, H. C.: Further Studies on Intoxication with Vitamin D, *Ann. Int. Med.* 10: 951 (Jan.) 1937.

Hench, P. S.; Bauer, Walter; Ghrist, David; Hall, Francis; Holbrook, W. P.; Key, J. A., and Slocumb, C. H.: The Present Status of Rheumatism and Arthritis: Review of American and English Literature for 1936, *Ann. Int. Med.* 11: 1089 (Jan.) 1938.

5. Dreyer and Reed.¹ Rappaport and Reed.² Reed.³ Rappaport, Reed, Hathaway and Struck.³

6. Bauer, Walter, and Ropes, M.: Unpublished data.

7. Bauer, Walter, and Short, C. L.: Unpublished data.

8. Bauer, Walter: The Parathyroid Glands in Health and Disease, *Virginia M. Monthly* 62:123 (June) 1935. Miles, L. M., and Fens, C. T.: Calcium and Phosphorus Metabolism in Osteomalacia, *J. Exptl. Med.* 41: 137 (Jan.) 1925.

9. Livingston.⁴ Farley.⁴ Steck.⁴ 10. Vrtiak and Lang.⁴ Holbrook and Hill.⁴ Wyatt, Hicks and Thompson.⁴

11. Holbrook and Hill.⁴ Hench, Bauer, Ghrist, Hall, Holbrook, Key and Slocumb.⁴

constant regimen employed prior to the institution of the form of therapy being studied. If each patient studied is so controlled, then one is best able to conclude whether the observed improvement or alteration in the course of the disease during and after treatment represents a therapeutic effect, a chance remission or the natural course of the disease. In all fairness to the form of therapy being studied, one should choose patients whose disease process is reversible. Any therapeutic measure employed in the treatment of rheumatoid arthritis should effect clinical improvement with great regularity in most patients before one has the right to suspect that one is dealing with a specific therapeutic

therapy was being employed. It is extremely difficult to draw conclusions from much of the data presented in the reports concerning the therapeutic effectiveness of large doses of vitamin D in rheumatoid arthritis because the patients were not rigidly controlled and the degree of improvement was not accurately recorded.

We have observed eighteen patients with typical rheumatoid arthritis prior to, during and after the administration of large doses of vitamin D. Only five (66, 90, 286, 328 and J. H.) of the eighteen patients were hospitalized during the period of treatment. From table 2 one notes that in all instances the arthritis was in a stationary or progressive state prior to the insti-

TABLE 1.—Results Observed by Other Authors Following the Administration of Massive Doses of Vitamin D to Patients with Rheumatoid Arthritis

Authors	Number of Patients	Daily Dose (U. S. P. Units)	Duration of Therapy	Other Measures Used	Per Cent Improved	Authors' Comments
Dreyer and Reed ¹	34*	200,000-500,000 occasionally up to 1,000,000	Not stated	Not stated	73†	Improvement evidenced locally by diminution of swelling and pain in the joints as well as by increased motion of the joints; general improvement consisted of improved nutritive state; greater muscular strength, less fatigability, improved gastrointestinal function and decreased vasomotor instability; "toxic symptoms often present without hypercalcemia"; "hypercalcemia often without associated toxicity"
Livingston ⁴	14	200,000-600,000	"Continued over an indefinite period of time"	Fever therapy in 9 cases	86‡	Improvement noted similar to that reported by Dreyer and Reed ¹ ; sedimentation rates reduced; "toxicity not associated with hypercalcemia"; "fever therapy in conjunction with vitamin D caused more rapid clinical improvement than vitamin D alone"
Farley ⁴	27§	200,000-600,000 in one case 1,000,000	Not stated	"Fever therapy in some"	100	Some patients treated for first time; others had received treatment elsewhere for as long as 5 to 6 years without benefit; decrease in pain, increased motion of the joints and improved nutritional state were observed; sedimentation rates lowered; roentgenograms showed recalcification of bone and reconstruction of cartilage
Vrtiak and Lang ⁴	20	150,000-200,000	Averages: 10 markedly improved group—3 months; moderately improved—10 months; slightly improved—7½ months; unimproved—3½ months	Not stated	60 (2 cases marked, 6 moderate, 4 slight)	Roentgenograms taken following completion of therapy failed to reveal increased bone density (5 cases); concluded that results are similar to those obtained with other forms of therapy; therefore believe conservative attitude should be maintained before vitamin D is accepted as a specific form of therapy
Wyatt, Hicks and Thompson ⁴	40	200,000-300,000	Not stated	General measures	20	Patients under observation for at least 6 months prior to treatment; improvement determined by bettered general physical status, decreased signs and symptoms of the joints; sedimentation rates, morphologic blood pictures, agglutination reactions for streptococci and serum calcium and phosphorus values were followed
Steck ⁴	?#	Usually 150,000-300,000 (some higher)	6 months' trial (with rest periods); continued beyond if improved	General measures	"75-80% can be benefited"	Noted improvement similar to that described by Dreyer and Reed ¹ ; also, decreased sedimentation rates and increased red blood cell counts; roentgenograms showed recalcification of bones
Holbrook and Hill ⁴	25	200,000-300,000	4 months	General measures	?	Noted less pain in 5 patients and marked reduction in sedimentation rates in 4; authors state that sufficient time has not elapsed to evaluate therapy
Hench et al. ⁴	"About 25"	250,000-600,000	1-2 years	Not stated	?	"Reduction in pain and soreness, and increase in well being in some patients; little change in articular lesions"

* Three other cases were listed as "mixed." These included one "infectious and gonorrheal" and two "menopausal and rheumatoid."

† Two of these three patients improved.

‡ Results in three cases listed as "still uncertain."

§ Improvement in four of the five patients treated with vitamin D alone, whereas eight of the patients treated with fever therapy in addition improved.

Author included all types of arthritis.

Number of patients treated not stated.

agent. In studies of this type it is equally important to record improvement as accurately as possible by every available method. This is best accomplished by recording separately subjective, objective and laboratory evidence of improvement as well as grading the final result on the basis of all three. This method of appraisal enables one to evaluate more accurately any psychic effect, such as is so frequently encountered in patients with chronic disease following the institution of any new form of therapy.

Failure to consider these many facts in times past has been responsible for many premature therapeutic and etiologic claims, the inspiring of false hope in patients at great financial expense and at times progression of the disease because a good general regimen was not adhered to during the time the new form of

tution of vitamin D therapy. It will be further noted that the duration of the arthritis, its severity and the extent of involvement varied from patient to patient. The observed therapeutic effects are recorded separately as subjective improvement, objective improvement, fluctuation in weight and alteration in the corrected sedimentation rate¹² as well as the total end result. Determinations of fasting serum calcium,¹³ serum phosphorus¹⁴ and serum phosphatase¹⁵ were made every

12. Rourke, M. D., and Ernste, A. C.: A Method for Correcting the Erythrocyte Sedimentation Rate for Variations in the Cell Volume Percentage of Blood, *J. Clin. Investigation* 8: 545 (June) 1930.

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TABLE 2.—Description of Patients with Rheumatoid Arthritis

Case; Sex; Age, Years	Characterization of Arthritis				Time Observed Before Therapy	Course During Pretreatment Period	Daily Dose of Vitamin D (U. S. P. Units)†	Duration of Therapy	Sedimentation Rates, Mm. per Hr.		
	Duration of Disease	Extent of Involve- ment	Activity of Disease	Total Severity					Just Prior to Therapy	During Therapy	Follow- up Therapy
32 ♀, 28	5 yrs.	Moderate	Moderate	Moderate	4½ yrs.	Slowly progressive	80,000 to 200,000‡	13 mos.	Low 0.63 High 1.11 Last 0.82	Low 0.45 High 0.58 Last 0.45	Not done
40 ♀, 61	7 yrs.	Extensive	Moderate	Moderate	4 yrs.	Stationary except for mild partial remission	60,000 to 160,000	7 wks.	Low 1.08 High 1.42 Last 1.19	Low 0.56 High 1.28 Last 1.14	1.0315 (4 mos.)
41 ♀, 64	8 yrs.	Mild	Mild	Mild	4 yrs.	Very slowly pro- gressive	(a) 20,000 to 160,000	5 mos.	Low 0.73 High 0.99 Last 0.65	Low 0.69 High 1.11 Last 0.63	0.7 (2 mos.)
							(b) 160,000 to 220,000	5 wks.	No rates done		
66 ♀, 17	9 yrs.	Mild	Moderate	Moderate	2 yrs.	Stationary	20,000 to 80,000	3 mos.	Low 1.64 High 1.97 Last 1.62	Low 1.45 High 1.56 Last 1.56	1.7 (2 mos.)
90 ♀, 49	7 yrs.	Moderate	Moderate	Moderate	2 yrs.	Slowly progressive	20,000 to 160,000	4 mos.	Low 1.67 High 1.94 Last 1.91	Low 1.34 High 1.70 Last 1.70	1.6214 (15 mos.)
120 ♂, 51	4 yrs.	Extensive	Marked	Severe	2 yrs.	Occasional periods of slight improve- ment; on the whole, stationary	20,000 to 160,000	10 mos.	Low 1.02 High 1.69 Last 1.59	Low 1.21 High 1.65 Last 1.21	1.3812 (3 mos.)
127 ♂, 26	10 yrs.	Extensive	Moderate	Moderate	4 yrs.	Slight progression of disease	80,000 to 160,000	15 wks.	Low 0.75 High 1.31 Last 1.25	Low 1.12 High 1.19 Last 1.12	1.4 (7 mos.)
181§ ♀, 29	7 yrs.	Mild	Mild	Mild	5 yrs.	Many good and bad periods; on the whole, stationary	80,000 to 160,000	11 mos.	Low 1.50 High 1.91 Last 1.52	Low 1.39 High 1.95 Last 1.95	1.631.0 (4 mos.)
194 ♂, 51	3 yrs.	Extensive	Moderate	Moderate	1½ yrs.	Practically station- ary; at times, slight improvement	80,000 to 160,000	5½ mos.	Low 1.78 High 2.03 Last 1.96	Low 0.96 High 1.59 Last 1.99	1.51.18 (7 mos.)
221# ♂, 60	25 yrs.	Mild	Marked	Severe	3 yrs.	Slowly progressive	80,000 to 160,000‡	8 mos.‡	Low 1.25 High 1.68 Last 1.33	Low 1.11 High 1.64 Last 1.63	1.4312 (6 mos.)
220§ ♀, 49	7 yrs.	Mild	Moderate	Moderate	4 yrs.	Slowly progressive	80,000 to 160,000	6 mos.	Low 0.63 High 1.12 Last 1.12	Low 0.53 High 0.84 Last 0.53	0.70 (7 mos.)
286 ♀, 21	5 yrs.	Moderate	Moderate	Moderate	6 mos.	Slowly progressive	(a) 40,000 to 200,000	3½ mos.	Low 1.42 High 1.69 Last 1.32	Low 0.53 High 1.03 Last 1.03	1.641.4 (3 mos.)
286	Because of relapse, treatment resumed 12 months later						(b) 120,000 to 300,000‡	4 mos.	Low 0.94 High 1.51 Last 1.22	Low 0.62 High 1.22 Last 0.63	0.54 (2+ mos.)
328 ♂, 42	6 yrs.	Extensive	Marked	Moderate	3 mos.	Stationary	80,000 to 160,000	1 yr.	Low 0.63 High 1.61 Last 0.63	Low 0.73 High 1.89 Last 1.00	Not done
335 ♀, 50	1 yr.	Extensive	Marked	Severe	2 mos.	Stationary	45,000 to 60,000	6 mos.	Low 1.15 High 1.45 Last 1.26	Low 0.78 High 1.63 Last 1.24	1.001.1 (2 mos.)
J. H. ♀, 11	2 yrs.	Moderate	Moderate	Moderate	6 mos.	Slowly progressive	48,000 to 60,000	3 mos.	Low 0.53 High 0.70 Last 0.56	Low 0.53 High 0.82 Last 0.67	0.430.7 (1½ mos.)
A. A. B.‖ ♂, 51	6 mos.	Extensive	Marked	Severe	6 mos.	Rapidly progressive	140,000 to 160,000	3 mos.	Low 1.59 High 1.78 Last 1.78	Low 1.53 High 1.72 Last 1.69	1.601.51 (3 mos.)
F. D.‖ ♀, 38	5 mos.	Mild	Mild	Mild	1 mo.	Slowly progressive	60,000 to 80,000	13 mos.	Low 0.63 High 0.81 Last 0.77	Low 0.59 High 0.72 Last 0.59	0.611.57 (3 mos.)
C. M.‖ ♀, 60	5 mos.	Moderate	Moderate	Moderate	5 mos.	Slowly progressive	250,000‡	6 mos.	Low 1.07 High 0.74 Last 1.05	Low 0.51 High 1.04 Last 1.15	1.170.55 (6 mos.)

* The numbers listed here refer to the patients with rheumatoid arthritis who have been studied in detail and have been reported in the past. These patients will be referred to by the same number in the detailed publications concerning rheumatoid arthritis which will appear later.

‡ These cases have been reported by the same number in the paper entitled "The Treatment of Rheumatoid Arthritis with Colloidal Sulfur."

This patient experienced complete remission for eighteen years. Present attack of seven years' duration.

Results Observed Following Treatment with Large Doses of Vitamin D

Toxic Manifestations		Observed Effects			End Results and Comments
Symptoms	Hyperealecemia, Mg. per 100 Cc.	Subjective Changes	Objective Changes	Weight Changes	
Nausea, epigastric discomfort	11.1 on 2 occasions	Joint symptoms not affected; fewer constitutional symptoms; stronger	None	Gained 14 pounds	Gained weight, some subjective general improvement; decreased sedimentation rate; no objective change
Nausea, vomiting, anorexia, diarrhea, headache	12.5 on 1 occasion—12 days after first appearance of toxic symptoms, 8 days after discontinuing vitamin D	None	None	Lost 4 pounds	No changes observed; sedimentation rate of 0.56 obtained at time of hyperealecemia; final sedimentation rate unaltered
None	12.0 on 1 occasion	None	None	Unchanged	No change in weight, sedimentation rate, or clinical condition
None	Not encountered	Less pain; slight general improvement	No change; one new joint (temporomandibular) became involved during therapy	Unchanged	Subjective improvement; one joint became involved for the first time during period of treatment; no change in weight or sedimentation rate
Nausea, vomiting, anorexia, epigastric pain	11.0 to 16.0, 12 weeks' duration	Less pain; slight general improvement	Slight reduction in joint swelling; slight increase in joint motion	Unchanged	Slight subjective and objective improvement; sedimentation rate not significantly altered; no weight change
"Indigestion"	11.8 on 1 occasion; became normal without altering dosage	Much stronger, less fatigue, less pain	More alert in appearance and activity; joint showed freer motion	Gained 6 pounds	Moderate subjective improvement; slight improvement objectively, mainly in general nutritive state; motions of joints freer, but soft tissue swelling and mobility unaltered; slight weight gain; sedimentation rate lowered
None	11.2 to 11.4, 3 weeks' duration	None	None	Unchanged	Far advanced ease with joint deformities; some joints of recent involvement; no change of any kind noted while under treatment; patient himself discontinued treatment because of disappointing results
Nausea, epigastric distress, anorexia, diarrhea	11.6 and 12.8 on 2 isolated occasions; 11.4 to 12.9, 3 months' duration; 12.0 to 11.1, 2 months' duration	None	None	Unchanged	Had exacerbation and remission while taking vitamin D; condition unchanged; sedimentation rate rose
Nausea, vomiting, heart burn, anorexia	12.8 to 12.9, 4 weeks; still 11.0, 15 days later 12.0, 1 additional occasion	Slight improvement in general strength; less joint pain	Slight reduction of joint swelling	Unchanged	Slight subjective and objective improvement; no change in weight or sedimentation rate; lowered sedimentation rate during therapy observed at time of hyperealecemia
Nausea, anorexia, frequency of urination, drowsiness	12.2 and 16.6 on 2 occasions	Improved at beginning (general strength, less pain); relapsed during course of treatment	None	Unchanged	Subjective improvement with onset of therapy, followed by relapse; no other type of improvement noted
Headache	11.7 on 1 occasion, dropped to normal without altering dosage	Improved at beginning; later relapsed	None	Unchanged	Large psychic element; subjectively improved at first, later discontinued therapy because of relapse; sedimentation rate decreased despite failure to improve
None	Not encountered	Marked improvement—less pain and stiffness; felt stronger and noted less fatigue	Marked improvement; reduction of swelling, disappearance of effusions, better joint motion	Gained 21 pounds	Marked improvement subjectively and objectively, with fall in sedimentation rate; gained 21 pounds; improvement lasted only a few weeks after therapy was discontinued
Nausea, epigastric discomfort, anorexia	11.9 and 12.0 on 2 occasions	Same improvement as experienced during first course but less marked and slower	Same as first course, but not so marked	Unchanged	During second period of therapy, subjective and objective improvement and drop in sedimentation rate noted; no weight change; improvement very slow
None	11.1 to 12.6, 4 weeks	Felt stronger and less pain at first; later relapsed to original state	None	Gained 10 pounds	Gained weight but showed no subjective or objective change at end of therapeutic trial; sedimentation rate higher at end
Nausea, epigastric distress	14.2 to 11.5, 12 weeks; 11.2 to 12.4, 13 weeks	Slight improvement in general strength	None	Unchanged	Except for slight subjective improvement, patient showed no change in condition; weight and sedimentation rate not altered
Anorexia	11.9 to 11.3, 2 weeks	None	None	Unchanged	Typical adult type of rheumatoid arthritis in a child; no change in clinical condition, weight or sedimentation rate while receiving therapy
None	11.2 to 11.9, 4 weeks	None	None	Unchanged	No change of any kind observed
Toxic symptoms persisted until the dose was reduced to 60,000 units	11.3 on 1 occasion	Moderate remissions and relapses while on a constant dose	Joint signs fluctuated markedly during treatment	Unchanged	Had moderate remissions and relapses while under treatment; final condition unchanged either subjectively or objectively; sedimentation rate fluctuated during course but final reading lower than pretreatment figure; no weight change
Marked anorexia, nausea and vomiting	11.6 to 12.5, 4 months	Slight subjective improvement	Swelling of wrists and fingers varied greatly during treatment	Lost 8 pounds	Slight subjective and objective improvement; general physical status and sedimentation rate unchanged

† Private patient of one of the authors (W. B.).

* Doses of 200,000 U.S.P. units and over were reached only with a preparation of vitamin D in sesame oil.

† Includes period of four months when drug was taken irregularly at the rate of about 20,000 to 80,000 U.S.P. units daily.

‡ In this column a indicates first course of treatment and b second course of treatment.

four to eight weeks in order to establish how often hypercalcemia resulted and whether or not suspected toxic symptoms occurred at the same time. Vitamin D¹⁶ in the form of Drisdol (1 drop = 250 U. S. P. units) was administered for a short time to the first five patients in the series. These and the remaining patients subsequently received a more concentrated preparation, crystalline vitamin D in propylene glycol (1 drop = 1,000 U. S. P. units) or in sesame oil (1 drop = 25,000 U. S. P. units). One third or one fourth of the total daily dose was administered with each meal, and the fourth (when given) was taken at bedtime. All preparations were administered in milk, because Lewis¹⁷ has shown that the antirachitic vitamin dissolved in propylene glycol is better utilized in the medium of milk than in the medium of corn oil. Throughout the period of study all patients were kept on a constant therapeutic regimen consisting of a high vitamin, high caloric diet (unless overweight), regular rest periods, daily physical therapeutic measures, vitamin B in the form of yeast and a constant ration of acetylsalicylic acid. No new therapy was added during the period of observation.

RESULTS

Subjective Improvement.—As can be seen from tables 2 and 3, if one were to judge solely on the basis of subjective improvement one might conclude that a good percentage of the patients with rheumatoid arthritis were benefited by vitamin D therapy. Subjective improvement, consisting of increased strength and feeling of well being, less of the myasthenia gravis-like fatigability and a reduction of pain and stiffness was reported by twelve of the eighteen patients. In four instances such improvement was short lived, being experienced only during the first few weeks of therapy. In the other eight cases such improvement was present throughout the period of treatment. In one instance it was marked, in another moderate, and in six slight. Such improvement was not maintained more than a few weeks following the discontinuance of vitamin D therapy.

Objective Improvement.—When evidence of improvement is judged on the basis of objective changes, one notes from tables 2 and 4 that only five of the eighteen patients experienced benefit from vitamin D therapy. These five patients had also experienced subjective improvement. In four the objective improvement was slight; in one it was marked. From table 2 it will be seen that the patient (286) in whom improvement was marked received large doses of vitamin D on two different occasions and each time experienced marked objective as well as subjective improvement. The improvement observed each time consisted of marked reduction of soft tissue swelling, disappearance or marked reduction of effusions of the knee joints and an increase in motion of the joints. In the other three cases the improvement was less marked and consisted of slight reduction of the soft tissue swelling and increase in motion of the joints. In one case (66) involvement of the new joints occurred during therapy. Two patients (F. D. and C. M.) experienced marked remissions and exacerbations of signs and symptoms in

the joints during the period of treatment, yet the dosage of vitamin D was kept constant throughout this time.

Weight Gain.—Improvement as measured by an appreciable weight gain (5 or more pounds) was observed in five patients (32, 120, 286, 328 and F. D.). Two of these patients (120 and 286) had noted subjective and objective improvement. Such beneficial effects were most marked in patient 286, who gained a total of 21 pounds (9.5 Kg.). Patients 32 and 328 had noted only subjective improvement, whereas Mrs. F. D. had exacerbations and remissions of both subjective and objective change.

Effect on the Sedimentation Rate.—From experience to date, the corrected erythrocyte sedimentation rate¹⁸ has proved to be the most reliable laboratory test for determining the activity of rheumatoid arthritis.¹⁸ This one objective laboratory test was performed at regular intervals before, during and after vitamin D therapy in order to determine whether the encountered variations in the sedimentation rate paralleled the observed clinical course of the disease.

In order to be consistent in judging when a decrease in the corrected sedimentation rate was significant, it was found necessary to follow some arbitrary rule.

TABLE 3.—Subjective Improvement

Marked improvement during entire period of therapy.....	1
Moderate improvement during entire period of therapy.....	1
Slight improvement during entire period of therapy.....	6
Improved only at beginning of therapy.....	4
No improvement at any time.....	6

TABLE 4.—Objective Improvement

Marked improvement	1
Slight improvement	4
No improvement	11

The one described here was finally adopted. In cases in which the sedimentation rate had varied between 0.5 and 1 mm. per minute a decreased rate was not considered significant unless it had fallen 0.15 mm. or more below the previously recorded rate. When the sedimentation rate had varied between 1 and 1.5 mm. per minute, a decrease of 0.2 mm. or more was considered significant. In cases in which the rate had been 1.5 mm. or more per minute a reduction was not considered significant unless it exceeded 0.3 mm. per minute.

In order to conserve space and yet give the reader some idea as to the changes observed in the curves of the sedimentation rate of each patient during the pre-treatment, treatment and follow-up periods, the maximal-minimal variations for each patient are presented in table 2. Detailed curves of the sedimentation rate of four patients are presented in the accompanying chart. From the chart and table 2 one notes that alterations in the curves of the sedimentation rate were observed in only seven of the eighteen patients, but in only five was it significant. In cases 120 and 286 (as seen in the chart and in table 2) subjective and objective improvement took place at the same time. In case 286 a reduction in the sedimentation rate and clinical improvement were noted each time vitamin D was administered. In

16. The Winthrop Chemical Company placed the vitamin D preparations at our disposal for this study.

17. Lewis, J. M.: Clinical Experience with Crystalline Vitamin D: The Influence of the Factor, J. Pediat. 6:

18. Short, C. L.; Dienes, Louis, and Bauer, Walter: Rheumatoid Arthritis: A Comparative Evaluation of the Commonly Employed Diagnostic Tests, J. A. M. A. 108: 2087 (June 19) 1937.

two other patients only subjective improvement was noted. The fifth patient, showing a lowered sedimentation rate, experienced no clinical improvement. Eleven of the remaining thirteen patients showed no significant alteration in the curve of the sedimentation rate. The sedimentation rates of the other two patients were increased, although both patients had considered themselves subjectively improved during the first weeks of therapy.

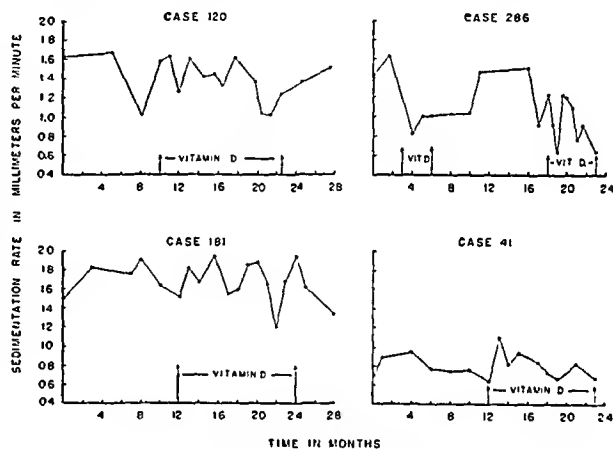
The observed changes in the sedimentation rates are difficult to interpret. That they cannot be of great significance is attested by the fact that both subjective and objective improvement was observed in only two of the eighteen cases studied. In fourteen cases the degree of variation encountered was as great in the pretreatment and follow-up periods as it was in the therapy period. In the chart, the variations in the curves of the sedimentation rates of the two patients who improved subjectively and objectively are compared with those of two patients who did not. These illustrated curves of the sedimentation rate serve to stress the fact that judging clinical improvement is extremely difficult even when a purely objective laboratory test is employed as the measuring stick. For instance, in case 120 the lowest sedimentation rate observed in the period of therapy was no lower than had been observed in the pretreatment period. One further observes that the sedimentation rate had begun to rise before vitamin D was discontinued. Although the changes observed in cases 120 and 286 may very well have been the result of vitamin D therapy, there is no denying the fact that they may represent, at least in part, the natural fluctuations that one frequently observes in patients receiving no specific therapy. Certainly one is not justified in drawing conclusions concerning improvement based on the sedimentation rate unless a significant sustained lowering takes place with some regularity in most patients during the period of therapy. Not having observed such an effect with any regularity in the eighteen cases studied, one is forced to conclude that vitamin D does not have any beneficial effect on the clinical course of rheumatoid arthritis as judged by the curve of the sedimentation rate. It was interesting to note that the greatest reductions in sedimentation rates frequently occurred at the time of the hypercalcemia. Such drops in the sedimentation rate were usually transient even though the hypercalcemia persisted. Variations of this type were encountered as often in those patients who did not experience clinical improvement as in those who did. This type of change in the sedimentation rate is probably directly related to the hypercalcemia and serves as further evidence that the variations in the sedimentation rates of erythrocytes cannot be ascribed to any one factor.¹⁹

Final Result and Duration of Improvement.—The improvement noted always took place slowly. The best clinical and laboratory results were observed in case 286. These were observed each time vitamin D was administered but were never sudden or dramatic. The patient was hospitalized throughout each course of vitamin D therapy. The beneficial results in this case as in the others were short lived. During the follow-up study it was noted that the arthritis gradually became as severe as it had been in the pretreatment period.

Such changes were obvious in a few weeks. The other three patients who had experienced subjective and objective improvement fared no better. In the fourteen cases not materially influenced by vitamin D the arthritis ran the same pretreatment course during and after the period of administration of vitamin D. Results such as these serve to emphasize the fact that follow-up studies are needed.

HYPERCALCEMIA AND VITAMIN D TOXICITY

The pretreatment calcium, phosphorus and phosphatase values of all eighteen patients were normal, indicating as have previous studies that the calcium and phosphorus metabolism of rheumatoid arthritic patients as judged by the blood examination is normal. In sixteen of the eighteen patients hypercalcemia developed at some time during the period of vitamin D therapy. From table 2 it will be noted that hypercalcemia was noted only on one or two occasions in nine of the eighteen patients. In five instances (32, 41, 120, 127 and 229) there were no significant associated symptoms of toxicity, and the serum calcium returned to normal without alteration of the dose of vitamin D.



These curves of sedimentation rates illustrate how difficult it is to interpret clinical improvement even though it is based on an objective laboratory test. Patients 120 and 286 experienced both subjective and objective improvement while receiving large doses of vitamin D, whereas patients 181 and 41 did not.

In cases 40, 221, 286 and F. D. either vitamin D was discontinued or the dose was reduced because of the degree of hypercalcemia or the severity of the toxic symptoms. In the other seven cases fasting serum calcium values varying from 11.2 to 16 mg. per hundred cubic centimeters persisted for weeks (from three to twenty-five) unless the dose of vitamin D was reduced or the drug discontinued. In most instances such values for hypercalcemia were not encountered until the dose was maintained between 160,000 and 200,000 U. S. P. units daily. However, a hypercalcemia of from 11.2 to 14.2 mg. per hundred cubic centimeters was observed in patient 335 for a period of twenty-five weeks, during which time the daily dose of vitamin D never exceeded 60,000 U. S. P. units. We were unable to exceed a dose of 200,000 U. S. P. units daily of the crystalline vitamin D in propylene glycol administered in milk without encountering toxic symptoms. Although the patients did tolerate larger doses of the crystalline vitamin D-sesame oil preparation, in no instance could we exceed a dose of 300,000 U. S. P. units daily without encountering serious toxic symptoms or hypercalcemia.

19. Ropes, Marion W.: Rossmels, Elsie, and Bauer, Walter: The Relationship Between the Erythrocyte Sedimentation Rate and the Plasma Proteins, *J. Clin. Investigation* 17: 520 (July) 1938.

The toxic symptoms observed were similar to those previously described,²⁰ consisting of anorexia, nausea, vomiting, epigastric distress or pain, diarrhea, headache, drowsiness, polyuria, polydipsia and nocturia. In some instances these symptoms were sufficiently marked to be alarming. Both the toxic symptoms and hypercalcemia often persisted for several weeks following discontinuance of the vitamin D therapy. An increased fasting serum phosphorus was observed on only two occasions. In these two instances values of 5.1 and 5.5 mg. per hundred cubic centimeters were observed with serum calcium values of 11.3 and 16.6 mg. In only one case did the serum phosphatase rise above a value of 5 Bodansky units. In this single instance a value of 6.5 units was observed with a normal serum calcium and phosphorus (10.2 and 3.4 mg. per hundred cubic centimeters respectively). As can be seen from table 2, the degree of hypercalcemia, its duration and the severity of the associated toxic symptoms were in no way related to the observed subjective and objective changes.

COMMENT

From the results observed in this series of patients with rheumatoid arthritis treated with large doses of vitamin D it is impossible to conclude that such therapy materially influences the course of the disease. Certainly the results are too disappointing to allow one to entertain the thought that one might be dealing with a specific therapeutic agent. If one were to judge solely on the basis of subjective and objective improvement experienced during the period of therapy only, one might be more enthusiastic concerning the value of vitamin D as a therapeutic agent for rheumatoid arthritis. When, however, a group of rheumatoid arthritic patients observed on the same constant general therapeutic regimen before, during and after the administration of large doses of vitamin D fail to show both clinical and laboratory evidence of improvement and no material alteration in the course of the disease, one is forced to conclude that the results are disappointing. Such an experience serves to stress the fact that each patient should serve as his own control and that adequate follow-up periods are necessary to judge the therapeutic results when one is dealing with a chronic disease such as rheumatoid arthritis. One might contend that beneficial effects are observed only while vitamin D is being administered. The data herein presented nullify such a contention. It might be argued that large doses of vitamin D are a useful addition to the therapeutic armamentarium employed in treating this disease. From our results we would conclude that the same general beneficial effects are experienced as often when vitamin D is administered in the usual therapeutic doses and that such dosages do not entail the risks attendant on hypercalcemia.

One might argue that failure to administer the same large doses of vitamin D employed by others is adequate reason for our not having obtained the same beneficial results previously reported. Evidence in favor of such an argument is readily obtained from tables 1 and 2, which show that only three patients in our series ever received a dose exceeding 200,000 U. S. P. units daily, whereas other workers have administered as much as 500,000 U. S. P. units or more daily. Because severe toxic symptoms or hypercalcemia were encountered in

all but three patients whenever the daily dose exceeded 200,000 U. S. P. units, we did not feel justified in employing larger doses. As can be seen from table 2, hypercalcemia was encountered more frequently than were toxic symptoms. Of these two complications of vitamin D therapy the hypercalcemia is the more serious, because if it is allowed to persist extensive calcium deposits and other pathologic changes may ensue.²¹

Other workers²² have reported that hypercalcemia and toxic symptoms are rarely encountered when large doses of vitamin D are administered, yet in our small series of patients receiving smaller doses hypercalcemia was observed in sixteen of the eighteen patients, and in seven cases it persisted for weeks unless the dose of vitamin D was reduced or the drug was discontinued. There appears to be only one possible explanation for such discrepancies, namely that the vitamin D preparation administered to the patients in this series was always given in milk. The medium of milk, according to the work of Lewis,¹⁷ allows for better utilization of a solution of crystalline vitamin D in propylene glycol than does the medium of corn oil (the medium employed by Reed and others). Lewis's results indicate that the antirachitic potency of such crystalline vitamin D preparations is increased tenfold when administered in milk. Whether a similar increased vitamin D potency resulted in our studies in consequence of the administration of the vitamin in milk we are unable to say with certainty. The high percentage of patients in whom hypercalcemia and toxic symptoms developed would suggest that such an increase in potency had occurred. If it did, then we were administering larger doses than the dosage in table 2 indicates. If this is true, the argument that failure to obtain better clinical results in this series was due to the employment of smaller doses no longer holds.

In order to be certain that the medium of propylene glycol might not be responsible for the high percentage of patients exhibiting toxic symptoms, this possibility was investigated. Propylene glycol was administered in milk to five patients in doses the same as or larger than they had received when taking the propylene glycol containing vitamin D. In no instance were any symptoms experienced; therefore this possibility is untenable.

Some workers²³ have contended that the simultaneous administration of yeast will aid greatly in controlling or preventing the toxic symptoms associated with large doses of vitamin D. Such was not our experience. As previously stated, all our patients received yeast throughout the period of observation, yet in a large percentage toxic symptoms developed.

No increased calcification or intra-articular changes were demonstrable roentgenographically in this series or others²⁴ following the administration of vitamin D. This is not surprising. We know that we are not dealing with a calcium and phosphorus deficiency disease and that the ability of articular cartilage to repair itself is at best very limited.²⁵ Therefore we are skeptical of statements²⁶ to the effect that filling in of

21. Rappaport, Reed, Hathaway and Struck.³ Steck, Deutsch, Reed and Struck.⁴

22. Dreyer and Reed.⁵ Livingston.⁶ Vrtiak and Lang.⁴

23. Reed.⁷ Livingston.⁶

24. Vrtiak and Lang.⁴

25. Bennett, G. A., and Bauer, Walter: A Study of the Repair of Articular Cartilage and the Reaction of Normal Joints of Adult Mice to Surgically Created Defects of Articular Cartilage. "Joint Mice" and Patellar Displacement, *Am. J. Path.* 8: 499 (Sept.) 1932. Bennett, G. A., and Bauer, Walter: Further Studies Concerning the Repair of Articular Cartilage in Dog Joints, *J. Bone & Joint Surg.* 17: 141 (Jan.) 1935.

26. Farley.⁴ Steck.⁴

20. Rappaport, Reed, Hathaway and Struck.³ Vrtiak and Lang.⁴ Steck, Deutsch, Reed and Struck.⁴ Hench, Bauer, Ghrist, Hall, Holbrook, Key and Slocumb.⁴

rarefied areas and reconstruction of articular cartilage in cases of rheumatoid arthritis have been observed in consequence of large doses of vitamin D.

Most therapeutic discoveries are soon acclaimed by others and the original reports of the discoverers substantiated by further and more detailed reports. As in the case of many other previously discovered antirheumatic remedies, such acclaim and substantiations have not appeared. Until they do, one is hardly justified in prescribing an expensive therapeutic agent capable of producing toxic symptoms and serious pathologic changes. For these reasons the Council on Pharmacy and Chemistry of the American Medical Association has been unwilling to include in New and Non-official Remedies Ertron and other high potency viosterol preparations as being specific in the treatment of arthritis.²⁷ If the beneficial results from vitamin D are to be ascribed to some impurity contained in the preparations employed, it had best be isolated and tested separately.

SUMMARY AND CONCLUSIONS

1. The effect of massive doses of vitamin D has been observed on eighteen patients with rheumatoid arthritis.

2. Observations prior to treatment showed that all the patients were in a stationary or slowly progressive state.

3. Subjective improvement lasting throughout the period of therapy was observed in eight cases. In only three instances was this accompanied by objective improvement and in only one was it marked. Such improvement was short lived when therapy was discontinued.

4. Only five patients showed a significant alteration in the curves of their sedimentation rate, and only two of these were improved subjectively and objectively.

5. Five patients gained weight during treatment.

6. Our results indicate that the administration of massive doses of vitamin D in rheumatoid arthritis is of little or no value in altering the course of the disease. The general effects of the larger doses do not appear significantly different from those observed with the usual therapeutic doses and do not justify the expense and dangers involved.

27. The Status of Certain Questions Concerning Vitamins, Reports of the Council on Pharmacy and Chemistry, J. A. M. A. 106:1732 (May 16) 1936; Condon and Ertron Not Acceptable for N. N. R., *ibid.* 109:132 (July 10) 1937.

Experiment and Then Think.—By 1850 Bernard's fame as an exponent of the experimental method in medicine began to be spread throughout Europe and overseas to the United States of America. At this time young physicians in America, as soon as they had taken their medical degrees, set out, if they were able, on the grand tour, and their principal objective was France rather than Germany. It is said that not only did they visit hospitals, their primary interest, but nearly all of them attended some of Bernard's lectures at the Collège de France, and a few engaged in experimentation under his direction. One of the best known American doctors of the nineteenth century, Weir Mitchell of Philadelphia, spent the year 1850-1851 in Paris, and, although he attended courses designed for surgical training, he wrote home that he liked Bernard's lectures in physiology and Robin's in microscopy much better. Bernard's pedagogical attitude is well illustrated in a conversation with Weir Mitchell. The latter had said that he thought so and so must be the case. "Why think," replied Bernard, "When you can experiment? Exhaust experiment and then think."—Olmsted, J. M. D.: Claude Bernard, Physiologist, New York, Harper & Bros., 1938.

SULFANILAMIDE IN THE TREATMENT OF BRAIN ABSCESS AND PREVENTION OF MENINGITIS

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The cure of a brain abscess and prevention of an almost certain hemolytic streptococcus meningitis by the administration of sulfanilamide has not been previously reported. Rowe¹ in a recent article describes two cases of brain abscess in which sulfanilamide constituted part of the therapy. The first patient had a pneumococcal (type V) abscess of the cerebellum which was treated also by surgical drainage and the administration of 220,000 units of appropriate pneumococcus antiserum. The second patient had a cerebellar abscess, culture of which revealed Friedländer's bacillus. The abscess was also treated by surgical drainage. As many instances of abscesses similar to these cured by drainage alone are known, as pneumococcus antiserum was used in case 1 and as sulfanilamide has not been shown to be effective against Friedländer's bacillus, as Rowe notes, it is impossible to credit sulfanilamide with the excellent result obtained in Rowe's cases.

In the case reported here the presence of a streptococcal cerebellar abscess was confirmed by culture of the pus obtained by aspiration, but the abscess was not drained. Furthermore the surface of the cerebellum, washed by cerebrospinal fluid and directly connected with the ventricular system and subarachnoid space, was contaminated with pus swarming with hemolytic streptococci. Certainly in the ordinary course of events a meningitis would have developed. Under sulfanilamide therapy there was no recurrence of symptoms attributable to the abscess, and no symptoms of meningitis ever appeared.

REPORT OF CASE

History.—F. S., a girl aged 4 years, referred to the University of Chicago Clinics by Dr. Joseph Brenemann of the Children's Memorial Hospital, was perfectly well until March 7, 1938, when she complained of a pain in her right ear. Her family physician was called. He prescribed some drops for instillation in the external auditory canal. The following day she had apparently completely recovered and continued to be well until March 29, when she suddenly complained of severe pain in her head. She vomited twice that evening. The pain and vomiting continued and she rapidly grew weak and was unable to walk. April 2 she was admitted to the Children's Memorial Hospital. There she was examined by a competent otologist, who could find no evidence of any disease in the ears. A lumbar puncture was made and the spinal fluid is reported to have contained 60 lymphocytes per cubic millimeter and 60 mg. of dextrose per hundred cubic centimeters. She was uncooperative and cried almost continuously. The head was retracted and drawn to the left so that the left ear almost touched the left shoulder. There was bilateral papilledema and deviation of the eyes to the left. All voluntary movements were ataxic, particularly those of the left extremities. A diagnosis of an expanding lesion in the left cerebellar hemisphere was made.

Examination.—She was transferred to the University of Chicago Clinics April 3 at 4 p. m. On admission here she was stuporous and cried out only when moved. The head was retracted and there was marked suboccipital tenderness. Definite early choking of the optic disks was present. The pupils were dilated and reacted poorly to light. The eyes were deviated to the left. The cranial nerves were otherwise normal.

From the Division of Neurology and Neurosurgery, University of Chicago.

1. Rowe, S. N.: The Use of Sulfanilamide in the Treatment of Brain Abscess, *Ann. Surg.* 107:620-626 (April) 1938.

The tendon reflexes were active throughout, though somewhat more marked on the right side. There was an unsustained ankle clonus on the left and the Babinski sign was present bilaterally. The response to pin prick was equal throughout. The right arm was moved very infrequently, whereas the left arm and the legs were moved freely and often. There was a definite hypotonia in the left extremities and some spasticity on the right. The temperature was 37.2 C. (99 F.), the pulse rate 120 and the respiratory rate 22 per minute. It was obvious that she was suffering from severely increased intracranial pressure. Accordingly it was decided to puncture the lateral ventricles and leave a T-shaped needle in place for continuous drainage. This was done at 10 p.m. on the day of admission by Dr. R. B. Cloward. The ventricular fluid was under markedly increased pressure, and drainage was profuse. Immediately after this procedure she became alert, recognized her father and talked readily and coherently. Subsequently examination revealed persistence of the papilledema and deviation of the eyes to the left with inability to move her eyes to the right beyond the midline. The tendon reflexes were active and equal. The Babinski sign was present bilaterally. She could move all four extremities and all were ataxic, though this condition was more marked on the right side, but otherwise the signs did not change. Roentgenograms of the skull revealed no separation of the cranial sutures. On admission the white

arachnoid space were wide open. Hemolytic streptococcus meningitis therefore seemed unavoidable. Soft rubber drains were inserted between the surface of the cerebellum and the muscles of the neck on both sides and the wound was closed.

Postoperative Course.—Sulfanilamide therapy was begun at once.² The patient was given 1.6 Gm. in 200 cc. of physiologic solution of sodium chloride by hypodermoclysis immediately and 0.3 Gm. by mouth as soon as she could swallow. The blood counts, sulfanilamide determinations of the blood and daily dosage of sulfanilamide are recorded in the accompanying table. A total of 49.9 Gm. of sulfanilamide was given between April 7 and May 11, i. e. in thirty-five days. The day following operation, April 8, the temperature rose to 39 C. (102 F.) but by April 10 it was back to 37 C. (98.6 F.) and remained between 37 and 38 C. (100.4 F.) thereafter.

The patient's condition immediately after the operation was good and continued so. There was profuse drainage of cerebrospinal fluid, and this was encouraged by keeping the patient flat in bed and forcing fluids as much as possible. Within two days (April 9) the amount of drainage was greatly reduced. April 10 the drain was removed from the left side. By April 12 all discharge of cerebrospinal fluid had ceased and the drain was removed from the right side. The abscess itself was never drained, these drains having been lying between the surface of the cerebellum and the muscles of the neck.

For two days following the aspiration of the abscess the inability to move the eyes to the right was still present, but this disturbance then disappeared. For a day or two the ataxia of the right arm persisted and then it too disappeared. By April 16 the neurologic examination was essentially negative.

On the sixth postoperative day (April 13) the patient was able to sit up in bed and feed herself. Eleven days after the operation she was able to be up in a wheel chair and four days later she was walking with assistance. She was soon running and playing about the corridors and playroom, seemed perfectly well and could have been discharged from the hospital any time after the fifteenth postoperative day. She was kept in the hospital, however, for observation and the administration of sulfanilamide as indicated in the table. She was discharged from the hospital May 15, thirty-eight days after the operation. Since her discharge she has been followed in the outpatient department of this and of the Children's Memorial Hospital. When last seen, August 30, she was perfectly well.

COMMENT

Contralateral Deviation of the Eyes.—One of the clinical manifestations in this case particularly excited our attention; to wit, conjugate deviation of the eyes to the side away from the abscess, with an inability to bring the eyes back beyond the midline. On reviewing our previous cases of cerebellar abscess I found one other case (B. S.) in which an abscess of the vermis and right cerebellar hemisphere was associated with a conjugate deviation of the eyes to the left. Row also presents two cases of abscess in the left cerebellar hemisphere with deviation of the eyes to the right. This sign is certainly not frequent in cases of cerebellar tumor, although it is not uncommon with tumors of the pons and may prove of value not only in localizing a cerebellar abscess but also in differentiating abscess from cerebellar tumor.

Sulfanilamide Therapy.—The efficacy of sulfanilamide in the treatment of hemolytic streptococcus infections is too well established to merit further discussion. That the sulfanilamide was effective in this case in preventing the development of a meningitis can scarcely be doubted. The cerebrospinal fluid space was contaminated with pus which on culture gave a heavy growth of these organisms. That they were highly virulent is clear from the pathologic changes already produced and the fact that the illness from the first

Course Under Sulfanilamide Therapy

Date	Red Blood Cells	Hemoglobin (Sahli), per Cent	White Blood Cells	Blood Sulfanilamide, Mg. %	Sulfanilamide per 24 Hours, Gm.
4/4	4.49	69	32,600
4/7	Aspiration of abscess				
	3.96	62	31,800	3.7
4/8	3.83	63	32,100	15.15	3.0
4/9	3.02	53	33,400	15.38	2.7
4/10	2.44	44	25,600	1.8
4/11	Transfusion of 200 cc. of citrated blood				
	3.11	60	18,550	7.10	1.8
4/12	3.65	63	15,500	1.8
4/13	3.86	65	11,950	9.5	1.8
4/14 to 4/17	1.8
4/18	3.94	69	14,150	6.00	1.8
4/19	3.76	77	14,650	1.8
4/20 to 4/26	1.2
4/27	4.52	71	13,850	4.60	1.2
4/28 to 5/5	1.2
5/6	4.85	80	2.90	1.2
5/7 to 5/10	1.2
5/11	2.60	1.2
Sulfanilamide discontinued					

blood cell count was 32,600 with 70 per cent polymorphonuclear leukocytes. The urine was normal and the Wassermann and Kahn reactions on the blood were negative.

Diagnosis.—It was felt that she had an expanding lesion of the left cerebellar hemisphere. The rapid progression and the reported pleocytosis in the spinal fluid pointed toward an abscess, but the absence of any demonstrable infection in the ear or elsewhere seemed against that diagnosis.

Operation.—April 7 the suboccipital region was explored. At first only the left lower limb of the usual curved suboccipital incision was made. A trephine opening was made in the bone and this opening enlarged. The dura was incised, the left cerebellar hemisphere, which was under considerable tension, being exposed. The subdural space was packed off with gauze soaked in a weak solution of iodine and the hemisphere explored with a needle. No abscess was found but at a depth of 2 cm. the needle encountered considerable resistance, which was interpreted as indicating the presence of a tumor. Accordingly the suboccipital incision was completed and the entire cerebellum was exposed. The right hemisphere was somewhat larger and softer than the left. A needle inserted into the medial part of this hemisphere again encountered resistance. The needle was then inserted laterally and encountered an abscess. Suction was immediately applied to the end of the needle and a large quantity of pus was removed. In spite of our efforts to prevent soiling of the field a drop of pus escaped about the needle onto the surface of the cerebellum. Smears of the pus revealed many small chains of cocci; subsequent culture yielded a heavy growth of hemolytic streptococci.

All communications between the surface of the cerebellum, the cisterna magna and the fourth ventricle and spinal sub-

2. Dr. Margaret Tingle of the Department of Pediatrics assisted in the administration of the sulfanilamide and repeatedly determined the concentration of the drug in the blood.

manifestation, ear ache, was of less than one month's duration and only of six days' duration from the onset of symptoms of the abscess itself until admission to this hospital.

The effect of the sulfanilamide on the abscess itself is perhaps not quite so clear. A considerable part, although undoubtedly not all, of the pus within the abscess was removed by aspiration on the one occasion in which the abscess was punctured, and furthermore suboccipital decompression was made. In the experience at this clinic³ no large abscess infected with hemolytic streptococci has ever been cured by a single aspiration. Kahn⁴ has had a similar experience. Dandy,⁵ on the other hand, intimates that cases of brain abscess (infecting organism not stated) have in his experience been cured by a single tapping, although he cites no particular instance. Grant and Groff⁶ have recently reported the apparent cure of a cerebellar abscess by a single tapping. They give no information, however, as to what the infecting organism was or whether the abscess was sterile. In spite of the uncertainty introduced by the experiences of Dandy and of Grant and Groff, it is very likely that the sulfanilamide was an important factor in preventing refilling of the abscess and recurrence of the symptoms in this case, as practically all neurosurgeons would admit that decompression and a single aspiration would but rarely, if ever, result in the cure of a hemolytic streptococcus cerebellar abscess.

Implications for Future Treatment.—In a recent publication³ the usual method of handling abscesses of the brain in this clinic has been presented. The procedure is briefly as follows: Drainage of the abscess is carried out in two stages. At the first operation a defect measuring 3 or 4 cm. in diameter is made in the skull overlying the abscess. The dura is incised. The subdural space about the opening is packed with gauze soaked in a weak solution of iodine. If the degree of increased intracranial tension is such as to demand immediate relief, a needle is inserted and pus is allowed to escape. Nothing further is done at this time. Two days later the pack is withdrawn from the subdural space. Six days after the first operation the wound is reopened, the abscess exposed, opened widely, evacuated and drained.

In view of the experience recorded here it is proposed in the future to begin the administration of sulfanilamide immediately after the first stage. A culture of the pus obtained will, of course, be taken and if the organism is a streptococcus or pneumococcus the sulfanilamide therapy will be continued. If the organism is a staphylococcus or some other organism not favorably influenced by this drug, sulfanilamide will be discontinued and the abscess drained as usual. If under sulfanilamide therapy the abscess does not refill and the patient continues to recover, no further surgical treatment will be attempted. If the abscess does refill, the drainage of the abscess can be carried out at a second operation, as has been done in the past. It is hoped that by this procedure a radical attack on the abscess with inherent damage to the surrounding brain tissue and dangers of extension of the infection will be avoided in some cases of abscess infected with hemo-

lytic streptococci and pneumococci. Attention should again be called to the possible toxic effect of sulfanilamide on the cells of the blood and therefore of the necessity of following the blood picture closely and of giving blood transfusions or of discontinuing the drug, as may be indicated.

SUMMARY

Owing to an error in diagnosis a right cerebellar abscess was exposed with a bilateral suboccipital craniectomy. The contents of the abscess were aspirated and the surface of the cerebellum was contaminated with pus swarming with hemolytic streptococci, thus exposing the ventricular system and the subarachnoid space to this infection. The abscess was not drained. The administration of sulfanilamide was begun at once. The patient improved steadily. There was almost no febrile reaction and at no time did signs develop either of meningitis or of refilling of the abscess. The patient had almost completely recovered within two weeks. In the future it is proposed to treat all brain abscesses in a similar manner; that is, make a defect in the skull over the abscess, aspirate the pus and begin the administration of sulfanilamide. If this suffices, nothing further will be done; if not, the abscess will be opened, evacuated and drained as usual.

950 East Fifty-Ninth Street.

Clinical Notes, Suggestions and New Instruments

PERIPHERAL NEURITIS FOLLOWING SULFANYLYL SULFANILAMIDE (DISULFANILAMIDE)

REPORT OF FOUR CASES

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AND

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Four cases presenting a characteristic picture of peripheral neuritis following the administration of sulfanylyl sulfanilamide (disulfanilamide) compounds were encountered at the Hospital of the University of Pennsylvania. Although these compounds are not at present proposed for general use in the United States, the cases are of interest. (It should be emphasized that this report concerns the use of sulfanylyl sulfanilamide and should not be construed to imply any similar toxicity of the widely used sulfanilamide compounds.)

REPORT OF CASES

CASE 1.—R., a white man aged 43, was admitted to the urologic service of the hospital Jan. 21, 1938. He had been under observation for a period of four years because of an established diagnosis of tuberculous cowperitis and cystitis. On reexamination the upper part of the urinary tract and the genital tract showed no evidence of tuberculous involvement. On cystoscopy, however, a generalized inflammatory reaction of the mucosa and an extensive pseudodiphtheritic membrane was observed. Culture of the urine was positive for diphtheroids and tubercle bacilli. In an attempt to free the bladder of the pseudodiphtheritic membrane the patient was given disulon, a brand of disulfanilamide, as a urinary antiseptic. For seven days (January 29 to February 5) he was given 45 grains (3 Gm.) a day; for eight succeeding days (February 5 to February 12) he was given 80 grains (5 Gm.) a day. The drug was discontinued because of increasing cyanosis and an intermittent febrile reaction. Subsequent routine culture of the urine was negative and cystoscopy revealed no membrane, although now the tuberculous ulcerations were apparent. There was no alteration of the blood picture.

Six days after the discontinuance of the disulon the patient complained of pain in the calves of both legs lasting two days.

From the Departments of Neurology and Urology of the Hospital of the University of Pennsylvania.

3. Bucy, P. C.: The Treatment of Brain Abscesses, *Ann. Surg.*, to be published.

4. Kahn, E. A.: The Treatment of Encapsulated Brain Abscess (discussion), *J. A. M. A.* 105:87-90 (Jan. 9) 1937.

5. Dandy, W. E.: The Brain, in Lewis, Dean: *Practice of Surgery*, Hagerstown, Md., W. F. Prior & Co., 1932, vol. 12.

6. Grant, F. C., and Groff, R. A.: The Surgical Treatment of Brain Abscess, *Pennsylvania M. J.* 41:597 (April) 1938.

Difficulty in walking was then noted, and examination revealed marked weakness in flexion and extension of the ankles and toes. Some time later the patient complained of slight weakness in the grip of both hands. Examination revealed slight impairment in the power of the flexors of the fingers and wrists, and considerable weakness, particularly in adduction, of the thumbs.

Electrical reactions March 14, twenty-four days after the onset of the weakness in the legs, disclosed an incomplete reaction of degeneration in the adductor pollicis muscles on both sides. The only change in the other muscles involved was a decreased excitability to faradic current. The diagnosis was peripheral neuritis, presumably due to sulfanilyl sulfanilamide.

There was slight improvement in power over a period of several weeks, although at the last examination, May 21, thirteen weeks after the onset, there was definite weakness of the adductors of the thumbs and weakness of the extensors and flexors of the ankle, so that the patient was unable to rise on his toes or heels.

CASE 2.—Z., a white man aged 22, was referred to the neurologic service of Dr. W. B. Cadwallader March 23, 1938. The patient contracted gonorrheal urethritis in August 1936 and was treated at that time with oral and subcutaneous medication for twelve weeks without subsidence of the discharge. He subsequently visited many clinics without relief.

From January to August 1937 he was treated intensively with local irrigations and prostatic massage. During this time repeated smears were positive for pus cells and gonococci. In August he received a course of sulfanilamide therapy starting with 60 grains (4 Gm.) a day. Smears continued to reveal positive results.

Feb. 14, 1938, uliron was given. He received nine tablets a day for one week and three tablets a day for the second week, the treatment ending February 28. One week later, March 7, pain and soreness of both calves were noted. Two days later this pain disappeared and at this time the patient noted loss of the power of flexion and extension of the ankles and toes. The gait was weak and staggering. He also noted weakness in the grip in both hands, and weakness in extension of the wrist. Most characteristic was marked weakness of adduction of the thumbs. There was no history of dietary deficiency or exposure to heavy metals.

Examination on admission revealed absent achilles tendon reflexes, increased sway when the eyes were closed, and step-page gait due to marked weakness of the flexors and extensors of the ankle. There was slight impairment of pain, temperature and vibratory sensation in the distal portions of all four extremities, weakness of the extensors and flexors of the wrists and fingers, marked weakness in the adductors of the thumbs, and slight wasting and loss of tone in the involved muscles.

Laboratory studies were negative. These included prostatic smears, spinal fluid studies, blood urea nitrogen, blood sugar, sedimentation rate, urinalyses and blood counts.

An attempt was made to determine any demonstrable effect of vigorous vitamin B₁ therapy. A controlled diet providing a minimal maintenance intake of vitamin B₁ was given from April 1 to April 24 inclusive. On April 7, 30 mg. of thiamin chloride (crystalline vitamin B₁ hydrochloride) was given intravenously. Examination three hours later revealed a subjective increase in the power of the grip on both sides. Dynamometer readings rose from 130 to 145 on the right, and from 125 to 135 on the left.

Over a period of seventeen days, 250 mg. of thiamin chloride was given intravenously in from 30 to 50 mg. doses. Very slight improvement appeared beyond that noted on the first day, and at the time of discharge, April 24, there was still definite weakness of adduction of both thumbs, and weakness of flexion and extension of the ankles and toes of about the same degree as on admission.

CASE 3.—L. W., a man aged 28, had acute gonorrheal infection in 1933. He first visited the urologic outpatient department of the hospital in September 1937, complaining of a urethral discharge of seven weeks' duration. A smear was strongly positive for gonococci. A course of sulfanilamide at that time was followed by relief of symptoms. April 12, 1938, the discharge reappeared. April 18, sulfanilyl sulfanilamide therapy was

started, and the patient received 40 grains (2.6 Gm.) a day until about May 12, at which time the medication was discontinued because of the appearance of pain in both calves followed by weakness of the lower legs and both thumbs. He complained that he could not wind his watch or button his shirt and that he "shuffled" when he walked. Examination disclosed absent achilles tendon reflexes, hypo-active patellar reflexes, marked weakness of flexion and extension of the toes and ankles, marked weakness of adduction of the thumb and radial deviation of the index finger of both hands. Electrical examination June 24 revealed reversal of the polar formula in the muscles of the thenar eminence and a slow type of response to galvanic stimulation. The anterior tibial muscles presented hypirritability to faradic stimulation. There was no demonstrable sensory change. Only slight improvement in power has been noted in the ten weeks since the onset.

CASE 4.—F. V., a man aged 67, with a diagnosis of carcinoma of the bladder, was started on sulfanilyl sulfanilamide therapy June 4 in an attempt to control a secondary infection of the bladder. He received 30 grains (2 Gm.) a day for six days and 40 grains (2.6 Gm.) a day for seven days, ending June 11. June 20 he experienced weakness in the right thumb and weakness of the feet in walking. Two days later there was weakness in the left thumb and both hands generally, so that he was forced to discontinue his work as shoemaker on June 23. Examination revealed marked weakness of adduction of the thumbs, ulnar and radial deviation of the index and middle fingers, and moderate weakness of flexion of the first three digits. There was no weakness of extension of the fingers or of wrist movements. The ankle jerks were absent. There was diminution in the appreciation of pain and vibratory sensation in the legs, which might well be accounted for by his age and varicosities of the leg veins. Moderate weakness of flexion and extension of the ankles and toes was present. There has been but slight improvement to date, one month after the onset.

COMMENT

Patient 1 has been seen frequently and at present, five months after the onset, has approximately 50 per cent of his former disability. Patient 2 is only slightly improved, according to a recent letter from the referring physician, Dr. W. F. J. Vogel of Riddlesburg, Pa., who has called our attention to recent articles in the German literature concerning neuritis following the use of the uliron brand of sulfanilyl sulfanilamide. This compound has enjoyed wide use in Germany and is reported as being very successful in the treatment of gonorrhea. Apparently the compound can be obtained by the public at the drugstore without the prescription of a physician.

Tietze¹ reports two cases of peroneal palsy due to uliron, characterized by weakness of the lower legs and pain in the calves. The achilles reflexes were absent. One patient presented weakness of the hands with atrophy of the interossei and the thenar and hypothenar muscle groups.

Lemke² presents five cases, strikingly similar to the four we have seen. All experienced pain in both calves and severe disturbance of gait. In all cases the achilles reflexes were absent. No abnormalities of sensation or electrical reactions were found. During the time of observation there was no improvement in any case. The total dosage of uliron varied approximately from 15 to 24 grains (1 to 1.5 Gm.) or more. The author stated that, as this complication occurred only in cases of gonorrhea, the neuritis might presumably be due to a toxin liberated by the destruction of the organisms. However, in the four cases cited in the present report, two were not cases of gonorrhea.

Euler³ reports a death due to uliron and points out other ill effects from the drug, manifested by leukopenia, dermatitis, fever, albuminuria and peripheral neuritis.

Hüllstrung and Krause⁴ describe severe polyneuritis in one case after the use of uliron and report that severe polyneuritis developed in pigeons fed with the same preparation.

1. Tietze, A.: *Periphere Lähmungen nach Ulironbehandlung*, München. med. Wehnschr. 85: 332 (March 4) 1938.
2. Lemke, R.: *Ueber Neuritis nach Ulironmedikation*, München. med. Wehnschr. 85: 482 (March 25) 1938.
3. Euler, H. E.: *Zur Ulironfrage*, München. med. Wehnschr. 63: 623 (April 29) 1938.
4. Hüllstrung, H., and Krause, F.: *Deutsche med. Wehnschr.* 64: 114-116 (Jan. 21) 1938.

Special Clinical Article

SENSITIVITY REACTIONS OF THE BLOOD AND BONE MARROW TO CERTAIN DRUGS

CLINICAL LECTURE AT SAN FRANCISCO
SESSION

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The idea that certain ordinarily useful drugs may, on repetition of normal doses, cause unexpected, profound and sometimes fatal idiosyncrasy reactions of the blood cells and hemopoietic tissues is relatively new. Prior to 1930 the nearest approach to this concept of drug allergy as a cause of serious hematologic injury was to be found in the literature of arsphenamine.¹ The older views of hematologic injury from drugs were based for the most part on supposedly orthodox toxic reactions.² These included anemia from poisoning by lead, mercury, arsenic, phenylhydrazine, trinitrotoluene, benzene and radium and methemoglobinemia from potassium chlorate, antipyrine, acetanilid, acetophenetidin, aniline and nitrobenzene. Although these reactions were viewed as toxic, it was recognized that individual susceptibility to such special effects existed, and to this extent something akin to idiosyncrasy was implied. After 1930, centering about the mystery of that relatively new disease called agranulocytic angina, there developed knowledge of hitherto unrecognized effects of acquired (drug) sensitivity involving the formed elements of the blood and bone marrow in very special and dramatic ways. The purpose of this presentation is to summarize and document the evidence on which this concept is based.

By way of definition the terms sensitivity, hypersensitivity and allergy are synonymous, and the term idiosyncrasy as here used means drug allergy. Drug allergy is considered to be a subdivision of general allergy, in which the same sequence is implied of prior, specific, sensitizing contact (probably mediated by a drug-protein combination)³ followed, on repetition of contact with the drug, by the allergic response. This type of response bears no (necessary) resemblance to the drug's normal pharmacologic and toxic action and may be precipitated by a trifling dose.

The problem presented by such acquired states of sensitivity has three sides; first, identification of the reacting agents or drugs; second, identification and study of the specifically conditioned responses of the sensitized subject, and, third, investigation of the conditioning factors responsible for the sensitization. The last phase must include investigation of the still inexplicable fact that only one person out of many thousands to whom the drug is administered becomes sensitized or conditioned.

The mechanisms of acquired drug idiosyncrasy and of human allergy in general are obscure. Why prior contact produces sensitization in one person and not in others is the fundamentally unsolved problem. One "answer" is hereditary predisposition. For present purposes this may be called genetic conditioning. This factor is apparent in certain types of hemolytic anemia and of thrombocytopenic purpura.

In the case of agranulocytic angina women predominate, and in a few instances a cyclic (presumably menstrual) incidence of attacks has been observed. A similar mechanism appears in certain cases of thrombocytopenic purpura. This illustrates what one may designate hormonal conditioning. To this should be added (hypothetic) dysfunction of the liver (as a major organ of detoxification) and of the spleen (as a most important site of destruction of red cells and platelets).

The fatigue state and traumatic shock (after dental extractions, accidents and operations) loom large in the background of agranulocytic angina. Other toxemias, including putrefactive disturbances and various bacterial and protozoal infections, have been suspected. These may be grouped as toxic conditioning factors.

Certain deficiency states are suspect. The experiments of Rhoads constitute a brilliant demonstration of the possibilities of conditioned toxicity of a drug (aminopyrine) and of a common metabolite (indole) in the causation of hemolytic anemia through the mediating effects of vitamin deficiency.

AGRANULOCYTIC ANGINA (PERNICIOUS LEUKOPENIA)

The remarkable malady known as agranulocytic angina or pernicious leukopenia, first adequately described by Schultz in 1922, is now almost universally believed to be caused by an acquired sensitivity of the leukocytes, endothelium and leukopoietic tissues to certain drugs and other allergens (or potential toxins).⁴ The pioneer observations which have established this point of view are those of Pepper,⁵ Kracke⁶ and Madison and Squier.⁷

The pathologic aspects of this disease include intimations of arrest of maturation, or anaknesis,⁸ of the leukocytes in their production centers, which I⁹ described in September 1931. To emphasize the analogies to pernicious anemia, which this condition in the bone marrow suggested, Krumphaar and I¹⁰ in 1932 proposed the designation pernicious leukopenia (instead of the etymologically objectionable and inaccurate terms that were and are employed). These analogies include the fact that the bone marrow in relapse in both diseases may be well supplied with progenitors of the cells which are lacking in the peripheral blood; the hemopoietic lesion in both diseases is reversible up to a certain point of terminal necrosis (or aplasia) of the bone marrow; the onset of remission in both is signalized by an outpouring of young cells from the bone marrow (the reticulocyte crisis in pernicious anemia and the

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Read in the Medical Section of the General Scientific Meetings at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 14, 1938.

1. Stokes, J. H.: *Modern Clinical Syphilology*, Philadelphia, W. B. Saunders Company, 1926, p. 315.

2. Ewing, James: *Clinical Pathology of the Blood*, Philadelphia, Lea Bros. & Co. 1901, pp. 96, 97 and 316. Pepper, O. H. P., and Farley, D. L.: *Practical Hematological Diagnosis*, Philadelphia, W. B. Saunders Company, 1933, pp. 343-351.

3. Landsteiner, Karl, and Jacobs, John: *Studies on Sensitization of Animals with Simple Chemical Compounds*, J. Exper. Med. 61: 643-656 (May) 1935.

4. (a) Fitz-Hugh, Thomas, Jr.: *The Etiology and Pathology of Agranulocytic Angina*, Am. J. Clin. Path. 7: 524-530 (Nov.) 1937. (b) Plum, P.: *Agranulocytosis*, London, H. K. Lewis & Co., Ltd., 1937.

5. Pepper, O. H. P.: *Leukopenia: A Review, with Special Reference to Agranulocytic Angina*, California & West. Med. 35: 173-199 (Aug.) 1931.

6. Kracke, R. R.: *Recurrent Agranulocytosis*, Am. J. Clin. Path. 1: 385-390 (Sept.) 1931.

7. Madison, F. W., and Squier, T. L.: *The Etiology of Primary Granulocytopenia (Agranulocytic Angina)*, J. A. M. A. 102: 755-759 (March 10) 1934.

8. Darling, R. C.; Parker, Frederic, Jr., and Jackson, Henry, Jr.: *The Pathology of the Bone Marrow in Agranulocytic Angina*, Am. J. Path. 12: 1-11 (Jan.) 1936.

9. Fitz-Hugh, Thomas Jr., in discussion on Waters, C. A., and Firor, W. B.: *Am. J. Roentgenol.* 27: 747-748 (May) 1932.

10. Fitz-Hugh, Thomas, Jr., and Krumphaar, E. B.: *Myeloid Cell Hyperplasia of the Bone Marrow in Agranulocytic Angina*, Am. J. M. Sc. 153: 104-110 (Jan.) 1932.

myelocyte crisis in pernicious leukopenia); the anaknesis of the red marrow in pernicious anemia is based on a conditioned deficiency mechanism as defined by Castle, and the leukocytic anaknesis of pernicious leukopenia is based on some sort of acquired sensitivity (perhaps comparable to the Shwartzman reaction¹¹), with certain drugs and possibly other substances acting as

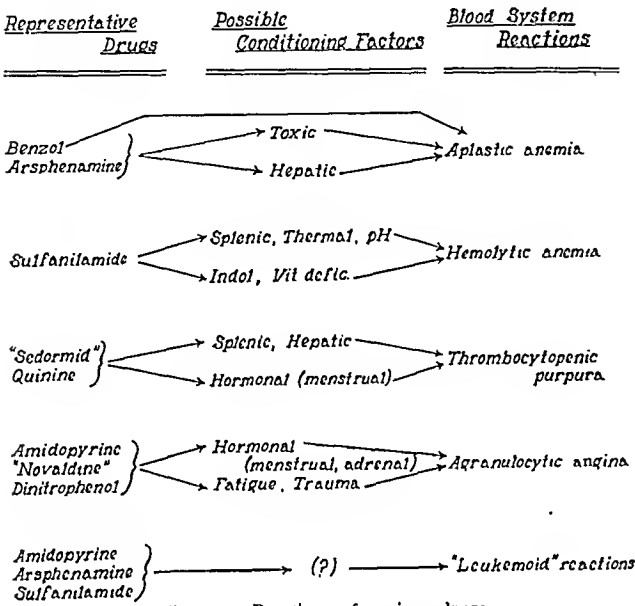


Chart 1.—Reactions of various drugs.

allergens or potential toxins in a perverse role, which I proposed in 1935 to designate as a mechanism of conditioned toxicity.¹²

Castle's concept of the conditioned deficiency has proved most fruitful. He showed that pernicious anemia is a deficiency disease which occurs despite normal diet, a specific starvation conditioned by a specific gastric defect. The picture thus invoked is like that of King Midas conditioned to starve in the face of plenty. I view the problem of drug allergy through the lens of Castle's hypothesis, somewhat enlarged and extended, as a mechanism of conditioned toxicity. Here the touch of King Midas conditions a result of poisoning or toxicity rather than of starvation or deficiency. When thus visualized, in sharper focus, the pattern of such mechanisms would seem to be composed of two interwoven threads, the one emanating from some drug or related substance (potential toxin or allergen) and the other representing influences which divert and modify the normal action pattern into an effect of conditioned toxicity.¹³

The drugs which have been suspected or proved to be idiosyncratic causes of individual attacks of agranulocytic angina are aminopyrine, dinitrophenol, arsphenamine and neoarsphenamine, gold salts, the diethylamine salt of stibanilic acid (neostibosan), acetophenetidin, sodium phenyldimethyl pyrazolon methylanomethane sulfonate (novaldin),¹⁴ a preparation containing about equal molecular parts of aminopyrine and 8-hydroxyquinoline-5-sulfonic acid

(causalin),¹⁵ quinine, cinchophen,¹⁶ bismuth, 5-phenyl-5-ethyl-hydantoin (nirvanol), plasmoquine 8-dimethyl-amino-iso-amyl 6 methoxyquinoline (plasmochin) and sulfanilamide.¹⁷ Other causes which I would classify as possible conditioning factors have been suggested: endocrine disturbance (estrus hormone, adrenal and hepatic), bacterial sensitization, cyclic toxemia (as with malaria, vaccination for typhoid) fatigue states, accidental and surgical trauma, genetic predisposition and vitamin deficiency.

In addition to the lesion of the bone marrow there is the phenomenon of the granulocytoclastic crisis,¹⁸ which has to be considered in any concept of the pathologic changes of agranulocytic angina. This sudden temporary disappearance of granulocytes (chart 2) from the circulation occurs too quickly to be mediated by a bone marrow arrest mechanism. I have suggested that it may represent a shock-conditioned "sticking" of leukocytes to the vascular endothelium such as E. R. Clarke has demonstrated in his glass window preparations in the rabbit's ear. One or more peripheral episodes of this kind may be a necessary prelude to the arrest status of the bone marrow in the disease proper. It is even conceivable that, for the duration of the disease, all granular and many nongranular leukocytes which emerge from the bone marrow, lymph nodes and spleen immediately become "stuck" to capillary endothelium, where they are engulfed and destroyed. If this peripheral depopulation of leukocytes can be proved it may remove the necessity for hypothesizing a maturation arrest as the primary mechanism.

The following case (chart 2) illustrates the granulocytoclastic crisis of acquired sensitivity to aminopyrine after recovery from agranulocytic angina.

CASE 1.—Miss R. N., aged 32, who had dysmenorrhea and menstrual migraine, had taken an occasional dose of a preparation of varying composition called midol,¹⁸ of 5 allyl 5 isopropylbarbiturate of aminopyrine (allonal) and of aminopyrine for several years without ill effects. Her present desperate illness, however, began after taking four tablets of

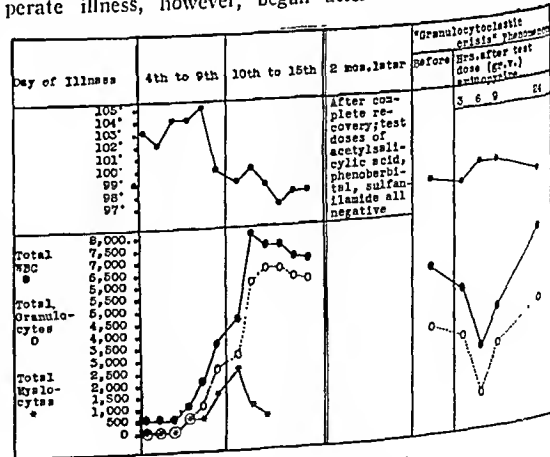


Chart 2.—Course in case 1.

allonal and some acetylsalicylic acid for menstrual cramp and "cold." She was given sulfanilamide but did not improve. A blood count on the fourth day established the diagnosis of agranulocytic angina. Recovery was inaugurated the ninth day.

11. Shwartzman, Gregory; Klemperer, Paul, and Gerber, I. E.: The Phenomenon of Local Tissue Reactivity to Bacterial Filtrates, *J. A. M. A.* **107**: 1946-1951 (Dec. 12) 1936.
12. Fitz-Hugh, Thomas, Jr.: Pernicious Leukopenia (Agranulocytic Angina): Clinical and Experimental Background and Present Status, *M. Clin. North America* **19**: 103-122 (July) 1935.
13. This is of course merely a restatement of the fundamental problem of all biologic reaction. It is useful only so far as it aids in the discovery and definition of conditioning factors.
14. Klumpp, T. G.: Agranulocytosis Associated with the Administration of "Novaldin," *J. A. M. A.* **108**: 637-638 (Feb. 20) 1937.

15. Jackson, Henry, Jr.: Two Cases of Agranulocytosis Following Ingestion of Causalin, to be published.
16. Shapiro, Shepard, and Lehman, Lester: Agranulocytosis Following Ingestion of Cinchophen, *Am. J. M. Sc.* **192**: 705-709 (Nov.) 1936.
17. Borst, J. G. G.: Death from Agranulocytosis After Treatment with Pronitil Flavum, *Lancet* **1**: 1519-1520 (June 26) 1937.
18. W. F. Curtis, F. G., and Koletsky, Simon: Fatal Granulocytopenia from Sulfanilamide, *J. A. M. A.* **110**: 368-370 (Jan. 29) 1938.
18. Midol, Bureau of Investigation, *J. A. M. A.* **110**: 1942 (June 4) 1938.

THROMBOCYTOPENIC PURPURA

The symptom complex of purpura, whether due to thrombocytopenia, to capillary damage or to both, may occasionally be traced to an allergic basis. It has long been known that certain drugs (notably iodides, phenolphthalein, barbiturates, benzene and arsphenamine) may cause a purpuric rash. For a good many years (since Glanzmann) the analogy of anaphylaxis has been invoked to explain certain types of purpura, under the designation anaphylactoid purpura. The modern concept,¹⁹ to which I would direct attention, is that of true thrombocytopenic purpura caused by an allergic reaction to certain foods and drugs. Here again one is reminded of the Schwartzman phenomenon.

The following case illustrates an interesting combination of conditioning factors, allergic, menstrual and splenic, which may exemplify some of the fundamental bases of so-called Werlhof's disease. This case also makes one consider the possibility that the spleen in this disease may produce a sensitizing substance, the removal of which is tantamount of nonspecific desensitization.²⁰

CASE 2.—A girl aged 16, who had had recurrent menorrhagia, epistaxis and hives for a year, showed on examination the classic picture of chronic thrombocytopenic purpura. The allergy survey disclosed a positive reaction to the cutaneous tests for pork, chocolate and grapefruit. Elimination of these substances was followed by moderate improvement. Test feeding with chocolate produced a drop in the platelet count from 50,000 to 20,000 within a few hours but no fresh purpura. However, later the patient ate some chocolate cake during menstruation. This was followed promptly by a fresh shower of purpura and exaggerated menorrhagia. (The suggestion here of a menstrually conditioned enhancement of the capillary platelet idiosyncrasy to chocolate is hard to deny.²¹) Despite subsequent adherence to orders this patient continued in a smoldering state of thrombocytopenic purpura, and after six months splenectomy was performed. The results were completely satisfactory, with disappearance not only of the hemorrhagic trouble but also of the hives even though she occasionally eats the forbidden foods.

Thrombocytopenic purpura due to idiosyncrasy to allylisovalerylurea (sedormid),²² quinine,²³ quinine and ergot,²⁴ acetophenetidin (phenacetin) and aminopyrine²⁵ has been reported in recent years. A study of bone marrow, spleen and other appropriate tissues in cases of this shocklike thrombocytopenic reaction is lacking.²⁶ In some of the cases positive cutaneous reactions were obtained. In others a drop in platelet content and a positive hemorrhagic exacerbation following a test dose of the drug served to prove the causal relationship. Here again the mechanism of sequestration (and destruction) of platelets caused by some widespread alteration of reticulo-endothelium is probably of primary importance. Possible conditioning factors in this

thrombocytopenic reaction pattern which have received serious consideration include dysfunction of the liver and spleen, cyclic menstrual hormone effects, genetic conditioning and vitamin deficiencies.

HEMOLYTIC ANEMIAS AND SO-CALLED APLASTIC ANEMIAS

The hemolytic effect of certain drugs, chemicals, toxins and serologic incompatibilities has long been known. Phenylhydrazine, trinitrotoluene, arseniuretted hydrogen (hydrogen arsenide) and n-propyl disulfide are supposedly direct hemolytic poisons. So too are snake venoms, saponins and certain bacterial toxins. The hemolytic effect of incompatible blood serum, of favism, of blackwater fever and of paroxysmal hemoglobinuria is in a different category. This mechanism is one of antigen-antibody reaction, related to immunity, anaphylaxis and allergy. Acute hemolytic anemia of this type occurs as an occasional idiosyncratic effect of sulfanilamide,²⁷ dinitrophenol, acetanilid and antipyrine in human beings; a probably similar mechanism produces the hemolytic anemia from aminopyrine and crystalline indole in dogs²⁸ specifically conditioned by a defective diet.

In addition to peripheral hemolysis, direct poisoning of the bone marrow, with consequent aplastic anemia, may be caused by drugs (lead, mercury, bismuth, arsenic, arsphenamine, benzene), by certain bacterial toxins and by radium and x-rays. It is becoming more and more obvious, however, that aplastic blood pictures do not always indicate aplastic marrow. There is often a marked discrepancy between the two.²⁹ The modern emphasis is shifting from the sterile hypothesis of primary aplasia to such factors as peripheral sequestration, destruction, loss, toxic arrest of maturation and breakdown of delivery mechanism, although it is still admitted that a terminal stage of fatty or aplastic marrow may result from any of these processes. The drugs that best illustrate this fact are arsphenamine³⁰ and sulfanilamide, which may produce hemolytic anemia, agranulocytosis, thrombocytopenic purpura or all three at once.

The work of Rhoads and Miller²⁸ is a brilliant pioneer elucidation of one of the (probably many) conditioning factors which may alter the normal pattern of drug effect. Their experiments prove that dogs conditioned by deficient diet (the blacktongue diet) become seriously anemic when given aminopyrine or crystalline indole, whereas not the diet or aminopyrine or indole alone is similarly effective. This work points clearly to the fact that not only a drug but also a common metabolite may, through the mediation of a conditioning mechanism, cause profound hemopoietic disturbance. Furthermore, these experiments will doubtless reopen the old problem of autointoxication, with the production and disposal of indole (and related substances) once more in the spotlight of clinical interest.

19. Squier, T. L., and Madison, F. W.: *Thrombocytopenia Purpura Due to Food Allergy*, *J. Allergy* 8: 143-155 (Jan.) 1937.

20. This is not a recommendation for splenectomy as a cure for the allergic state in general (or even as the treatment of choice in all cases of Werlhof's disease).

21. Minot, C. R.: *Purpura Hemorrhagica with Lymphocytosis*, *Am. J. M. Sc.* 192: 445-456 (Oct.) 1936. Brinck, Joachim, and Patrunsky, Max: *Hyperovarian Hemorrhagic Diathesis*, *Deutsche med. Wchnschr.* 63: 386-388 (March 5) 1937.

22. Loewy, F. E.: *Thrombocytopenic Hemorrhagic Purpura Due to Idiosyncrasy Toward the Hypnotic Sedormid*, *Lancet* 1: 845-848 (April 21) 1934.

23. Beiglböck, Wilhelm: *Ein Fall von thrombopenischer Purpura bei echter Chininüberempfindlichkeit*, *Ztschr. f. klin. Med.* 131: 308-316, 1937.

24. Peskin, M. M., and Miller, J. A.: *Quinine and Ergot Allergy and Thrombocytopenic Purpura*, *J. A. M. A.* 102: 1737-1740 (May 26) 1934.

25. Krawiec, R. R.: *Thrombocytopenic Granulocytopenia*, *Southern M. J.* 25: 448-455 (March) 1932.

26. An exception to this statement is the study of the sternal marrow by V. Hadorn (Schweiz. med. Wchnschr. 66: 1273-1276 [Dec. 12] 1936) who, contrary to the majority of observers, expressed the opinion that this effect of sedormid is specifically toxic and not idiosyncratic, despite the fact that in one of his cases the condition developed after only two tablets of sedormid.

27. Harvey, A. M., and Janeway, C. A.: *The Development of Acute Hemolytic Anemia During the Administration of Sulfanilamide*, *J. A. M. A.* 109: 12-16 (July 3) 1937. Jennings, G. H., and Southwell-Sander, G.: *Anemia and Agranulocytosis During Sulfanilamide Therapy*, *Lancet* 2: 898-901 (Oct. 16) 1937. Kohn, S. E.: *Acute Hemolytic Anemia During Treatment with Sulfanilamide*, *J. A. M. A.* 109: 1005-1006 (Sept. 25) 1937. Long, P. H., and Bliss, Eleanor A.: *Use of Sulfanilamide*, *South. M. J.* 50: 479-487 (May) 1937.

28. Rhoads, C. P.: *Effect of Indole on Hematopoiesis in Dogs Fed Deficient Diets*, *Proc. Soc. Exper. Biol. & Med.* 36: 652-654 (June) 1937. Rhoads, C. P., and Miller, D. K.: *Effect of Diet on Susceptibility of Canine Hematopoietic System to Damage by Amidopyrine*, *ibid.* 36: 654-656 (June) 1937.

29. Rhoads, C. P., and Barker, W. H.: *Refractory Anemia*, *J. A. M. A.* 110: 794-795 (March 12) 1938. Zanaty, A. F.: *Sternal Puncture in Pernicious and Achromic Anemia*, *Lancet* 2: 1365-1367 (Dec. 11) 1937.

30. Brenfen, I. D., and Singerman, Isidor: *Acute Aplastic Anemia Complicating Arsphenamine Therapy*, *J. A. M. A.* 98: 1725-1725 (May 14) 1932.

the gravity of the disorder under treatment. It is also well to avoid unnecessary combinations of drugs known to have similar idiosyncratic potentialities. Frequent blood counts should be made when hematologic idiosyncrasy may be anticipated. Finally, when therapy with potentially dangerous drugs is necessary, careful attention should be given to the patient's nutrition and general vital status.

The treatment of the damage, once initiated, is best accomplished by rigid prohibition of all probable medicinal offenders. The first rule is "primum non nocere." Palliative therapy should be limited to a few agents such as sodium bromide, sodium salicylate, codeine sulfate or a little morphine. An appropriate vitamin supply should be insured. Parenteral injection of liver extract, crystalline vitamin B₁ and ascorbic acid may be used instead of, or in addition to, oral therapy. Transfusions of blood are sometimes life saving. The new yellow bone marrow concentrate for oral administration is, I believe, of real value in the treatment of agranulocytic angina. Iron, calcium, bile salts and hydrochloric acid are sometimes indicated. The intravenous administration of dextrose or saline solution is often helpful. Even splenectomy has a place in an occasional case of thrombocytopenic purpura of apparently allergic type (case 2) and in an occasional case of refractory anemia of the type discussed by Rhoads and Barker.²⁰

Since patients with serious hemopoietic injury are easy prey for "opportunistic bacteria," their treatment may occasionally warrant specific serotherapy or chemotherapy. Such therapy is justifiable if the invading organisms are of a single predominating strain against which a truly specific agent is available and if the invasion has assumed serious proportions (e. g. septicemia or pneumonia). I have observed the successful termination of secondary hemolytic streptococcus septicemia with sulfanilamide therapy in a case of aminopyrine-induced agranulocytic angina^{4a} and in a case of pancytopenia of undetermined cause, despite the fact that sulfanilamide has itself been incriminated as a cause of agranulocytosis and pancytopenia. It is important to remember that the patient may succumb, even after hematologic remission is well under way, to infection acquired during relapse.

CONCLUSIONS

1. Specific hematologic reaction patterns of acquired sensitivity to certain drugs constitute a relatively modern observation.
2. These reaction patterns include certain cases of agranulocytic angina, thrombocytopenic purpura, hemolytic anemia, pancytopenia and leukemoid reactions.
3. These idiosyncratic effects of drugs (and possibly other acquired allergies) may advantageously be viewed as conditioned toxicities.
4. The fact that certain drugs, through mechanisms of acquired sensitivity, may produce these disorders suggests that other substances (food, bacterial products and metabolites) may occasionally behave in a similar fashion.
5. The search for possible factors which may condition hematologic sensitization has led under various circumstances to suspicion of disorders of the liver and spleen, states of vitamin deficiency, genetic factors (atopy), endocrine influence, intestinal putrefaction, states of fatigue and shock and prior hemopoietic disease.

2016 DeLancey Street.

Special Article

THE MEASUREMENT OF AIR CONDITIONS

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AND

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DETROIT

With the advent of an increasing use of artificially conditioned atmospheres in office buildings, auditoriums, department stores, apartment buildings and to some extent individual dwellings, it appears desirable to have some physical means of anticipating the reactions of a group of persons to a given set of air conditions. The individual may have facilities at his command to regulate indoor air conditions according to his personal needs or desires, but comfort air conditioning for a large group is successful only when satisfaction is obtained for the majority of occupants.

The physician, the layman, the engineer, in fact every one entrusted with the control of or called on to judge the suitability of air conditions, should understand the use of modern instruments designed to supplement the ordinary and very often inadequate "dry-bulb" thermometer and should be familiar with the optimal conditions for human comfort and efficiency as indicated by these more reliable instruments, so far as they are known at this time.

It is our intent in this report to describe some of the more important instruments and charts devised for this purpose and to appraise the reliability of various measures of atmospheric conditions as indexes of human comfort over a wide range of conditions.

In the first report of this committee¹ it was pointed out that there are five principal factors determining the quality of the air and its effect on human comfort: air temperature, humidity, air movement, radiation and cleanliness of the air.

The early concept of an adequate index of environmental warmth was simply the air temperature as indicated by an ordinary mercury-in-glass or alcohol-in-glass thermometer. Air temperature even now is considered a fairly reliable measure of warmth when the factors humidity, air movement and radiation vary within a narrow range. The difficulty of creating satisfactory air conditions on the basis of temperature alone has stimulated extensive research during the past two decades to determine, if possible, a convenient single index combining the effects of temperature, humidity, air movement and radiation. The major requirement of such an index is that it should correlate well with the human response to a wide range of air conditions. As secondary considerations, it should not be too difficult to determine or compute, nor should it require too complex or cumbersome instruments for its measurement.

Before discussing the more successful combined indexes of warmth and comfort that have been developed, we shall review separately air temperature,

From the Bureau of Industrial Hygiene, Detroit Department of Health. This is the sixth in a series of reports prepared by the American Medical Association's Committee to Study Air Conditioning. Members of the committee are William F. Petersen, Chicago; Constantin P. Yaglou, Boston; Emory R. Hayhurst, Columbus, Ohio; Horatio B. Williams, New York, and Carey P. McCord, Detroit, chairman.
1. Yaglou, C. P.: *Physical and Physiologic Principles of Air Conditioning*. J. A. M. A. 108:1708 (May 15) 1937.

humidity, air movement and radiation with particular reference to the instruments used for their measurement.

AIR TEMPERATURE

Air temperature, technically known as "dry-bulb" temperature, is usually measured by an ordinary glass thermometer which is not affected by the humidity of the air. Since the glass bulb of the ordinary mercury or alcohol thermometer is affected by radiant heat, it should be shielded from the "view" of objects or surfaces whose temperatures are much above or below the air temperature. As an alternative, the thermometer bulb can be silvered to reflect radiant heat. Gas thermometers, electrical resistance thermometers and thermocouple instruments are inherently laboratory or industrial devices and cannot replace the simpler liquid-in-glass type for air conditioning applications. Bi-metallic elements are used in some types of indicating or recording thermometers, but in general they are not as sensitive to small changes of temperature as the mercury or alcohol thermometers.

HUMIDITY

"Absolute humidity" is the amount of water vapor present in the air. It is usually expressed in grains of moisture per cubic foot or per pound of air (7,000 grains = 1 pound).

By definition, "relative humidity" is the ratio of the actual partial pressure of the water vapor in the air to the saturation pressure at the dry-bulb temperature. For practical purposes, relative humidity is taken as the ratio of absolute humidity to the maximum amount of water vapor that a given volume of air will hold at the given dry-bulb temperature, since this ratio is approximately the same as the ratio of vapor pressures. The capacity of the air for holding moisture varies directly with dry-bulb temperature. For example, a cubic foot of air can hold 1.3 grains of moisture at 20 F., 8 grains at 70 F. and 20 grains at 100 F.

Determination of Humidity.—The humidity of the air is usually determined by means of a "sling psychrometer" (fig. 1). This consists of a dry-bulb and a wet-bulb thermometer mounted side by side on a metal strip pivoted to a handle. The cloth wick covering the wet bulb is moistened, preferably with distilled water, and the instrument is whirled at a peripheral speed of 1,000 feet or more per minute. The wet-bulb

thermometer is read at frequent intervals until the lowest temperature is obtained. Knowing the dry-bulb and wet-bulb temperatures, either the absolute or the relative humidity can be determined easily from "psychrometric" tables or charts. The lower the moisture content of the air, the greater will be the difference between the dry-bulb and wet-bulb temperatures (this difference is called "wet-bulb depression"). In a saturated atmosphere, on the other hand, no evaporation would be possible, and the wet-bulb thermometer would therefore show the same temperature as the dry-bulb thermometer.

In a motor driven psychrometer, the air is blown across the wet bulb by a small fan. Stationary wet-bulb hygrometers in which no provision is made for the rapid ventilation of the wet bulb are subject to great errors. Carrier and Lindsay² explain this fact as follows:

Without unusual precautions, the stationary hygrometer is an exceedingly unreliable instrument for even the most ordinary work, since the drafts and convection currents existing in a heated room are uncertain and consequently the corrections to be applied are uncertain. This is particularly to be emphasized since the errors on a stationary wet-bulb thermometer occur on the most sensitive portion of the correction curves; i. e., at the very low velocities. It is shown, for instance, that the error of the stationary wet-bulb thermometer will vary from about 5 per cent at 120 F. to 33 per cent at 32 F. In ordinary room conditions velocities from zero to 50 feet per minute may exist without being . . . noticed as a draft. At a 50 degree wet-bulb temperature, the error will vary from 24 per cent in still air to 9 per cent at 50 feet per minute.

Human hair, wood, cellulose materials, goldbeaters' skin and paper impregnated with deliquescent salts are among the hygroscopic substances that have been used as the expanding and contracting elements of humidity control devices or dial indicators. Most hygrometers of this type need frequent recalibration particularly following exposures to unusual conditions, which often produce large after-effects and which may cause permanent damage. Such hygroscopic humidity indicators are satisfactory when frequently checked or recalibrated against a standard sling psychrometer. Gravimetric or volumetric chemical methods are sometimes used in the laboratory for determining humidity, but they are more laborious than sling psychrometer methods.

Dew-Point Temperature.—This is an important hygrometric factor from the standpoint of moisture condensation. It is the temperature to which a given sample of air must be cooled in order that condensation of the water vapor within it may begin. When air is at the dew point, the dry-bulb, wet-bulb and dew-point temperatures are identical. If the air is cooled below the dew point, some of the water vapor will condense and all three temperatures will be correspondingly lowered. This is actually what takes place on window glass in cold weather or when the air is dehumidified by cooling in an air conditioner. The temperature of the cold surface or substance must be slightly below the dew-point temperature of the air before condensation can occur thereon.

The dew-point temperature is usually determined from sling psychrometer readings by means of a chart or table. Direct determinations of the dew point for the estimation of relative or absolute humidity are subject to considerable errors and are seldom used in place of wet-bulb determinations.

2. Carrier, W. H., and Lindsay, D. C.: The Temperature of Evaporation of Water into Air, Tr. Am. Soc. Mech. Engrs. 46: 739, 1924.

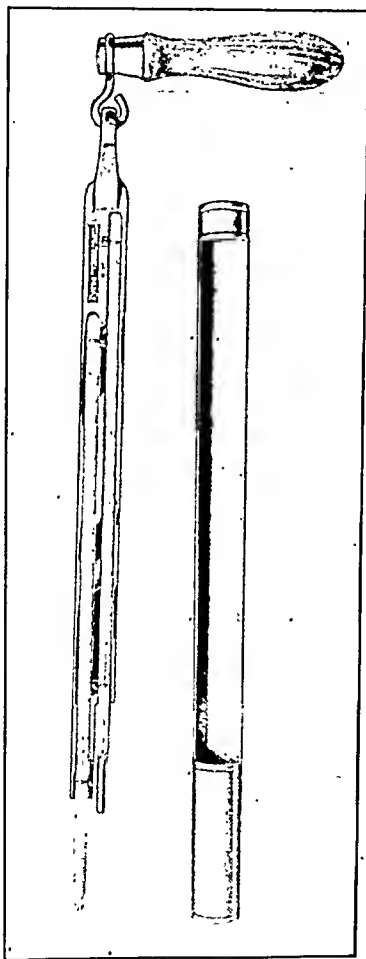


Fig. 1.—Sling Psychrometer (courtesy Taylor Instrument Companies).

AIR MOVEMENT

About a century ago Heberden³ and Reid⁴ pointed out that the ordinary thermometer alone is not reliable as an indicator of comfort and suggested that air movement as well as air temperature should be measured in estimating the relative comfort of various air conditions. The value of air movement in relieving discomfort arising from high air temperatures or intense radiation is now well known.

Air Movement in Rooms.—It is frequently desirable to trace the course and destination of the air supplied to a room or to determine the source and direction of drafts. Several simple devices are available, such as small paper or cloth flags, silk threads, small balloons, candle flames, tobacco smoke or smoke clouds generated by hand aspirated smoke tubes of the Bureau of Mines type.⁵ In these smoke tubes, air is forced by a rubber aspirating bulb through a glass tube containing pumice stone saturated with anhydrous tin tetrachloride or titanium tetrachloride, and a dense white cloud issues from the tube and travels with the air currents. A similar smoke cloud device produces a dense ammonium chloride fume by combining, in a small Y nozzle, the ammonia and hydrogen chloride gases from separate small bottles containing these gases in solution.

Of particular importance in comfort air conditioning are the continuously changing turbulent air currents which vary in velocity from 10 to 100 feet per minute and which defy measurement by any type of purely mechanical anemometer. In fact "air movement," as used in combination with temperature, humidity and radiation in this report, means the summated or integrated movement of air across a body from all directions. Thermal types of anemometers are well suited for integrating turbulent air currents, and the instrument most widely used for this purpose at present is the "katathermometer."

Standard Katathermometer.—Early in the nineteenth century Leslie,⁶ and a few decades later Heberden,³ used thermometers for measuring air velocities utilizing apparently the same principle as that of the modern katathermometer (fig. 2). This instrument was introduced by Hill⁷ in 1914 as a physical instrument with possibilities of simulating to some degree the dynamic function of the body in losing heat by radiation, convection and evaporation. It is now generally accepted that neither the dry nor wet "kata cooling powers" are adequate indexes of comfort, since their response to air conditions differs in several ways from the response of the human body to the same conditions.⁸ Air currents exert a greater cooling effect on the relatively small bulb of the katathermometer than on the human body. The human body, under ordinary conditions, is neither completely dry, as the dry katathermometer,

nor completely wet, as the wet katathermometer, and therefore does not react the same as do these two instruments. Only under special limited conditions will the dry and wet katathermometers give reliable indications of human response to air conditions.

Because of its sensitivity to air movement the dry katathermometer is valuable as an anemometer, provided the walls and objects surrounding the instrument are at substantially the same temperature as the moving air. If the bulb of the katathermometer is silvered, errors due to radiation between the bulb and its surroundings usually can be neglected. By determining both the air temperature and "kata cooling power" of the air, air movement can be computed from equations or obtained more conveniently from the calibration chart (fig. 3) developed by Yaglou and Dokoff under accurately controlled air conditions.



Fig. 2.—Katathermometer (courtesy R. E. P. Elmer, Winnetka, Ill.).

The katathermometer is a specially constructed alcohol thermometer, with a cylindric bulb about three quarters of an inch in diameter and $1\frac{1}{2}$ inches long. The stem is 8 inches long, and ordinarily it is etched at only two points, 95 and 100 degrees F. An enlargement of the bore at the top of the stem serves as a safety reservoir in case of accidental overheating and also permits the instrument to be heated in a vacuum bottle considerably above 100 F. so that by the time its bulb is dried and suspended in the desired position it has acquired a uniform rate of cooling. The time required for the alcohol meniscus to fall from the 100 to the 95 degree mark is then observed, and the "kata factor" marked on the stem of the instrument by its manufacturer is divided by this time in seconds, giving the "cooling power" of the air in millicalories per square centimeter of bulb surface per second at a mean temperature of 97.7 F.

A high temperature katathermometer which cools from 130 to 125 F. is useful in determining air velocity when the air temperature exceeds 90 F.⁹

Electrical Anemometers.—Several types of electrically heated instruments are available, all depending in principle on the cooling of a hot body. Among these are Hill's electrical katathermometer,¹⁰ several types of "hot wire" anemometers,¹¹ Hill and Griffith's "calometer,"¹² Weeks' "coolometer,"¹³ a thermocouple anemometer¹⁴ and Yaglou's "heated thermometer

3. Heberden, William: An Account of the Heat of July 1825, Together with Some Remarks upon Sensible Cold, Phil. Tr. Roy. Soc. London, 1826, pt. II, p. 69.

4. Reid, D. B.: Illustrations of the Theory and Practice of Ventilation, London, Longmans, Brown, Green & Longmans, 1844.

5. Katz, S. H., and Bloomfield, J. J.: Sulfur Trioxide Smoke Tubes for Determining Air Currents, Report of Investigations 2505, U. S. Bureau of Mines, July 1923.

6. Leslie, J.: An Experimental Inquiry into the Nature and Propagation of Heat, London, J. Mawman, 1804.

7. Hill, Leonard: (a) Report on Ventilation and the Effect of Open Air and Wind on the Respiratory Metabolism, Report of the Local Government Board of Public Health, No. 100, New Series, 1914. (b) The Science of Ventilation and Open-Air Treatment: Part I, Special Report 32, Medical Research Council (Great Britain), London, H. M. Stationery Office, 1919-1920. (c) The Katathermometer in Studies of Body Heat and Efficiency, Special Report 73, Medical Research Council (Great Britain), 1923.

8. McConnell, W. J., and Yaglou, C. P.: The Katathermometer: Its Value and Defects, Pub. Health Rep. 39: 2293 (Sept. 5) 1924; Bureau of Mines, Report of Investigations, No. 2565, 1924.

9. Angus, T. C.; Hill, Leonard, and Soper, H. E.: A New Katathermometer for Hot Atmospheres and a Simplified Method of Computing, J. Indust. Hyg. 12: 66 (Feb.) 1930.

10. Hill, Leonard: An Electrically Heated Katathermometer and Comparison of Wet Kata with Wet Bulb, Proc. Physiol. Soc., J. Physiol. 53: 84 (Jan. 31) 1920.

11. Ower, E.: The Measurement of Air Flow, London, Chapman & Hall, Ltd., 1927.

12. Weeks, W. S.: A New Instrument for Measuring Cooling Power—The Coolometer, J. Indust. Hyg. 13: 261 (Sept.) 1931.

13. American Instrument Company, Inc., 8010 Georgia Avenue, Silver Spring, Md.

anemometer."¹⁴ Although these instruments are noted for their sensitivity to low air velocities, either the elaborate apparatus required for their use or the convection currents caused by their own heating elements, or both, have detracted much from their usefulness, with the possible exception of the heated thermometer anemometer.

The heated thermometer anemometer (fig. 4) is a low temperature hot wire instrument possessing many

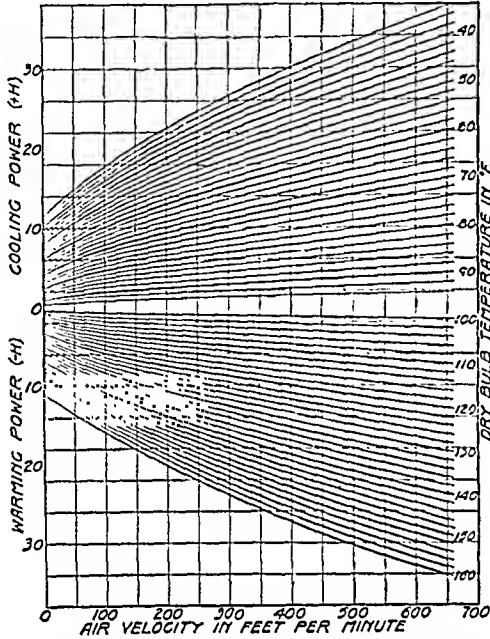


Fig. 3.—Chart for determining air velocity from readings of the standard katathermometer (Yaglou, C. P., and Dokoff, K.: Calibration of the Katathermometer Over a Wide Range of Air Conditions, *J. Indust. Hyg.* 11: 278 [Oct.] 1929).

of the desirable characteristics of the conventional hot wire anemometers and much of the simplicity of the standard katathermometer. The temperature of the wire is only from 10 to 40 degrees F. above the air temperature and it is indicated on an ordinary thermometer, around the bulb of which the wire is wound. Small dry cells furnish the heating current, and the voltage is regulated by a rheostat; this auxiliary apparatus can be assembled in a small box. The readings to be observed are the temperatures of both the heated and an unheated thermometer together with the voltage used. Air velocity is obtained by a table or chart or is computed by an equation. By varying the voltage one can measure accurately any air velocity between 10 and 6,000 feet per minute. The instrument automatically compensates for ordinary variations of air density due to temperature changes and is negligibly affected by humidity, radiant heat and convectional currents of its own. It offers little or no obstruction to air flow but requires correction for partial immersion of its stem when used in small pipes.

Mechanical and Pressure Type Anemometers.—For measuring air velocities much above 100 feet per minute that have definite and constant direction, the rotary vane anemometer (fig. 5) is convenient. It consists of a small windmill geared to a tachometer, which counts the number of revolutions and is calibrated to indicate directly the number of feet of air that have passed through the vanes over a measured period of time.

The vane anemometer is used principally at the face of registers or grilles to determine the air velocity through the grilles and thereby the flow of air through the room. It is also extensively used for the measurement of air flow in mines and tunnels. This type of anemometer usually registers a velocity that is within 10 per cent above or below the true velocity, but if the instrument is not cleaned and calibrated frequently its error may be as high as 30 or 40 per cent.

Another instrument for the measurement of unidirectional air currents is the swinging vane direct-reading velocity meter of the type shown in figure 6. Air entering one side of the instrument impinges on a counterbalanced vane directly connected with the scale pointer and leaves through a port on the opposite side. The advantages of this type of velocity meter are that no observation of elapsed time is required, instantaneous readings are possible and usually no computations are necessary. Variable air velocities below 100 feet per minute cannot be determined accurately by this type of meter. For high velocity readings, special adapters, orifices or jets with rubber tube connections are attached to the air inlet and outlet ports, and the range of usefulness of the meter can be extended to the measurement of air velocities inside ventilating ducts.

There are several other types of air metering devices, such as pitot tubes, venturi tubes and orifice meters¹⁵ that are commonly used by engineers for air flow measurements inside ventilating ducts, but these are outside the scope of this report.

Rate of Air Change in Rooms.—The rate of air change in confined spaces may be determined by measuring the air flow in the supply duct to the room or by measuring the concentration of carbon dioxide at different points in the breathing zone of an occupied room. The advantages of the second method are that

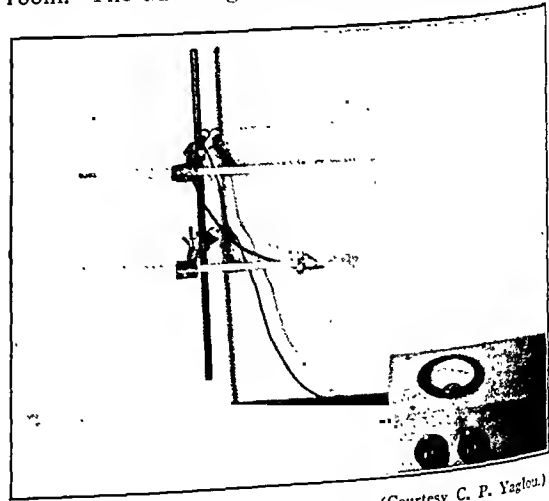


Fig. 4.—Heated thermometer anemometer. (Courtesy C. P. Yaglou.)

it also takes into account leakage of air through window and door openings, and it affords an estimation of the distribution of air to various parts of the room. Haldane's apparatus¹⁶ or Petterson and Palmquist's apparatus is commonly used for measuring carbon dioxide concentrations. The amount of outdoor air supplied to the room in cubic feet per minute per occu-

14. Yaglou, C. P.: The Heated Thermometer Anemometer, *J. Indust. Hyg. & Toxicol.*, to be published.

15. Haldane, J. S., and Graham, J. I.: *Methods of Air Analysis*. London, Charles Griffin & Co., Ltd., 1935.

pant is computed from the following equation, assuming that each person produces 0.6 cubic foot of carbon dioxide per hour:

$$\text{C. F. M. per occupant} = \frac{100}{(\text{CO}_2)_i - (\text{CO}_2)_o}$$

Where $(\text{CO}_2)_i$ = average concentration of carbon dioxide in room in parts per 10,000 and $(\text{CO}_2)_o$ = concentration in outside air, usually assumed at 3 parts per 10,000

Wells¹⁶ has recently described a bacteriologic method of determining air change in rooms by atomizing a dilute liquid culture of *Bacillus coli* into the air and determining the rate of disappearance of the bacilli by means of his centrifuge. The number of air changes per hour was found to be equal to the difference between the natural logarithms of the counts of two successive samples divided by the elapsed time in hours between the two samples.

RADIATION

All bodies are continuously radiating heat to one another, and those which remain at a constant temperature are receiving as much heat as they lose. Although heat transferred by radiation passes through the intervening air, it is, for practical purposes, independent of the physical properties of the atmosphere.

Radiation of heat between two objects is proportional to the difference between the fourth powers of their absolute surface temperatures (Stefan-Boltzmann law) and also to the emissivity of the surface. A perfect "black body" has an emissivity of 1, while a highly polished metallic surface may have an emissivity as low as 0.02.

Occupants of a room are subjected to "positive" radiations from radiators or warm objects and "negative" radiations to cold windows or walls. The sum of all positive and negative radiations is usually expressed in terms of the "mean radiant temperature."

In crowded spaces such as classrooms, auditoriums and theaters, the heat lost by radiation from the bodies of occupants to the walls and surroundings is reduced considerably because of counter radiation between persons closely assembled. A lower air temperature, lower humidity or increased air movement may therefore be required to offset the decrease of heat loss by radiation under such conditions.

Radiation from any given source can be accurately estimated by directing a bolometer, radiometer or thermopile to receive the radiation from that source.

The bolometer offers a small absorbing surface of about 3 square inches of hard black enamel covering a coil of platinum wire around a thin mica plate. The change of electrical resistance of the coil on exposure to radiation is measured, and from this can be determined the intensity of the radiation per square foot per hour.¹⁷

The Crookes radiometer is an instrument for detecting and measuring radiant energy by converting it into the mechanical energy of a small rotating vane mounted in an evacuated glass bulb. Each blade of the vane presents a reflecting surface as it approaches the source of radiation and an absorbing surface as it travels away from the source.

The thermopile is a series of small thermocouples whose combined potential differences, indicated by a

sensitive galvanometer, are a measure of the intensity of radiation striking the exposed ends of the thermocouples.

INSTRUMENTS COMBINING RADIATION-CONVECTION EFFECTS

Radiation meters such as the three just described are not suitable for frequent determinations of the mean radiant temperature because a great number of readings must be taken in order to integrate radiation from all directions. Moreover, these radiations must be suitably combined with the convective cooling power of the air in order to estimate the relative warmth of different environments, excluding humidity effects. Various instruments have been devised especially for this purpose. Under ordinary conditions of warmth during the heating season when humidity is somewhat unimportant, the human body response to

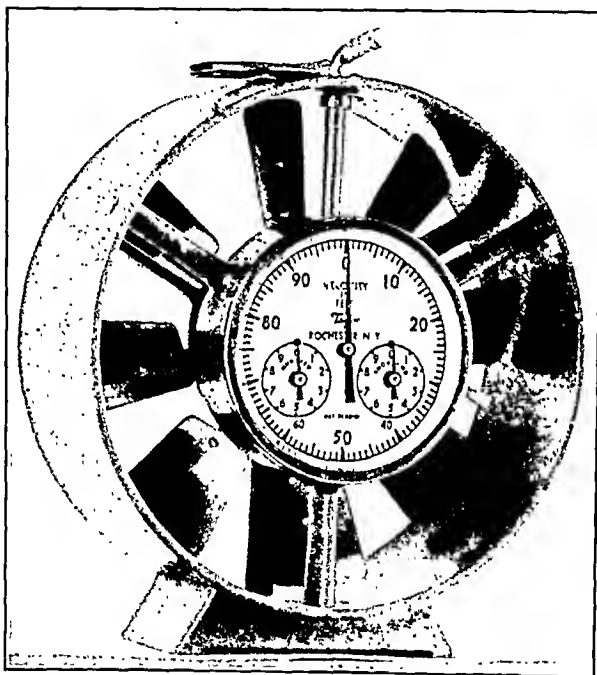


Fig. 5—Rotary vane anemometer (courtesy Taylor Instrument Companies).

environmental change is somewhat like a physical instrument, and sensations of warmth follow closely the indications of suitably designed radiation-convection meters. Outside the comfort zone, however, where definite physiologic reactions are manifested, all physical instruments fail to some degree because it is too difficult to simulate human response to heat and cold.

Unheated Globe Thermometer.—The unheated globe thermometer¹⁸ is the simplest of all radiation-convection instruments that have been proposed as indicators of environmental warmth. It consists of a 6 inch blackened copper sphere containing an ordinary thermometer with its bulb at the center of the sphere. Owing to convection effects, its temperature reading usually lies between the air temperature and the mean radiant temperature of the surroundings and indicates only whether the mean radiant temperature is higher or lower than the air temperature. It is best suited

16. Wells, W. F., and Wells, M. W.: Measurement of Sanitary Ventilation, *Am. J. Pub. Health* 28: 343 (March) 1938.

17. Bone, W. A.; Callendar, H. L., and Yates, H. J.: A Bolometric Method of Determining the Efficiencies of Radiating Bodies, *Proc. Roy. Soc. London, Series A* 91: 245, 1915.

18. Vernon, H. M.: The Measurement of Radiant Heat in Relation to Human Comfort, *J. Indust. Hyg.* 14: 95 (March) 1932.

to rooms heated by radiant methods. In rooms heated by convection methods the surface temperature of the globe is far below the surface temperature of the human body. The instrument tends to underestimate negative radiations to cold walls and windows. In some cases the resulting globe temperatures may be misleading. For example, if wall temperatures are below the air temperature, the globe reading in "still" air will be lower than the air temperature; but if the air is set in motion, the globe thermometer will rise to approach the air temperature. Thus, in the latter case the globe thermometer indicates apparently warmer conditions when, in fact, the increase in air movement usually has just the opposite effect on the human body. When the walls and air are at the same temperature, the globe records the air temperature and is not at all affected by air movement.

As pointed out by Bedford and Warner,¹⁹ the globe thermometer in itself is inadequate as an index of the thermal environment, but if the dry-bulb temperature and air movement are determined along with globe thermometer readings it is possible to compute

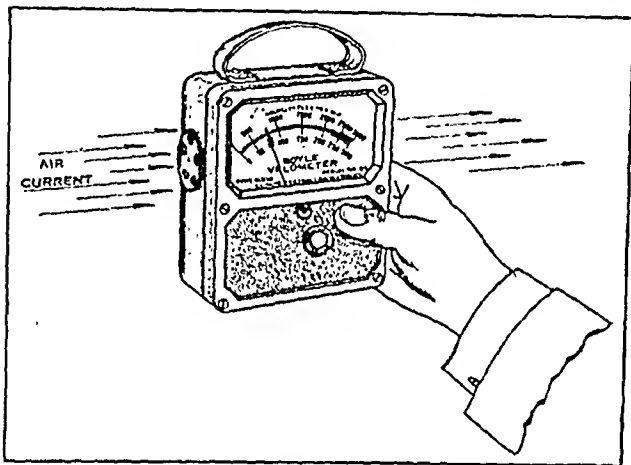


Fig. 6.—Swinging vane direct-reading air velocity meter (Velometer—courtesy Illinois Testing Laboratories, Inc.).

either the "equivalent temperature" or the mean radiant temperature of the environment from equations developed by these investigators.²⁰ The equivalent temperature of a thermally nonuniform environment is defined as the temperature of a thermally uniform enclosure (walls, furnishings and air at the same temperature) in which, under still air conditions, a "sizeable" black body loses heat at the same rate as in the nonuniform environment. This is a very useful quantity in air conditioning, as it combines mean radiant temperature and air temperature into a single value.

Heated Globe Thermometer.—Some of the drawbacks of the unheated globe may be overcome by heating it so as to make its rate of heat loss by radiation and convection per unit surface area comparable to that of the human body. Yaglou²¹ constructed such a heated globe using two or three hollow concentric spheres for equalizing the outside surface temperature of the instrument. The outer sphere is 6 inches in diameter and painted a dull black; the inner sphere is

4 inches in diameter and contains an electrical heating element which is normally adjusted to produce a heat loss of 15.3 British thermal units per hour per square foot of surface of the outer globe. This is the rate of heat loss by radiation and convection in an average adult under usual sedentary conditions. An ordinary glass thermometer with its bulb adjacent to the inside of the outer globe gives the instrumental reading with little time lag. The readings of such a globe seem to correlate well with the sensations of warmth and comfort induced by various environmental conditions, and such readings can be utilized in computing equivalent temperature or mean radiant temperature of the environment.

Thermo-Integrator.—Winslow and Greenburg's "thermo-integrator"²² operates on the same principle as the heated globe except that instead of an ordinary thermometer it utilizes thermocouples for measuring the mean temperature of the surface from which heat loss takes place.

The instrument consists of a blackened hollow cylinder 8 inches in diameter and 24 inches high with hemispherical ends. The cylinder is evacuated to less than 0.1 per cent of atmospheric pressure to minimize convection currents and air stratification within the instrument and thereby maintain a more uniform surface temperature. A nichrome wire filament inside the cylinder furnishes heat at the rate of 17.5 British thermal units per square foot per hour. Eight thermocouples distributed over the surface of the instrument are arranged in a parallel circuit and connected to an automatic recorder so as to obtain a continuous record of the average surface temperature.

Eupatheoscope.—Dufton's eupatheoscope²³ is essentially a cylinder 7½ inches in diameter and 22 inches high, which is heated from the inside by electrical elements. Preliminary studies indicated that a body of this size was necessary to imitate faithfully the responses of the human body to the effects of radiation. The current input to the elements is measured and controlled to maintain the cylinder surface temperature at 75 F.,²⁴ as indicated by several suitably distributed thermocouples embedded in the surface. The equivalent temperature is determined from the heat input necessary to maintain the cylinder at 75 F. This particular instrument cannot be used at temperatures above 75 F.

The principle of operation of the eupatheoscope is the reverse of that of the thermo-integrator and the heated globe. Instead of constant heat production and variable surface temperature as is practically the case in the human body, the eupatheoscope functions with variable heat input and approximately constant surface temperature. Lately Dufton²⁵ reconstructed his instrument providing for a variable surface temperature in accordance with studies made by Bedford on a large number of persons. Details of the new eupatheoscope are not as yet available, but it is hoped that it will afford a more representative index of human response and that its useful operation will be extended to temperatures above 75 F.

19. Bedford, T., and Warner, C. G.: The Globe Thermometer in Studies of Heating and Ventilation, *J. Hyg.* 34: 458 (Dec.) 1934.

20. Bedford, T.: The Measurement of Environmental Warmth, *Tr. Inst. Mining Engrs.* 94: 76, part 1, 1937-1938.

21. Yaglou, C. P.: A Heated Globe Thermometer for Evaluating Environmental Conditions of Comfort and for Studying Radiation-Convection Effects, *J. Indust. Hyg.* 17: 185 (Sept.) 1935.

22. Winslow, C. E. A., and Greenburg, L.: The Thermo-Integrator—A New Instrument for the Observation of Thermal Interchanges, *Heating, Piping & Air Conditioning* 7: 41 (Jan.) 1935.

23. Winslow, C. E. A.; Greenburg, L.; Moriyama, I. M., and Rodde, E. J.: The Calibration of the Thermo-Integrator, *Am. J. Hyg.* 22: 137 (July) 1935.

24. This is supposed to be the temperature of a person at rest under comfortable conditions in England.

25. Dufton, A. F.: The Equivalent Temperature of a Warmed Room, *J. Inst. Heat. & Vent. Engrs. (London)* 4: 227, 1936.

The eupatheoscope is a valuable laboratory instrument, but it is expensive and too cumbersome for field determinations of the equivalent temperature. For this purpose Dufton²⁶ has suggested the use of two katathermometers, one with a silvered bulb and the other with a blackened bulb, both having a cooling range of from 75.5 to 74.5 F. The time of cooling of these special katathermometers is recorded on a special stop watch. These two readings added together give approximately the equivalent temperature of the environment.

In the original work in England a room was assumed to be comfortably warmed when the eupatheoscope lost heat at the rate of 17.5 British thermal units per hour per square foot of external surface. The surface temperature of the instrument was maintained at 75 F. In the United States, where convection type of heating rather than radiant heating is used, where clothing is lighter and indoor air temperatures are kept higher, Willard and others²⁷ have used 15.4 British thermal units per hour per square foot with the surface temperature at 83 F. (the accepted mean surface temperature of the human body in this country at the comfortable temperature of 73 F.) as the standard of comfort to be indicated by the eupatheoscope.

RADIATION DURING THE HEATING SEASON

Under ordinary living and working conditions in this country the extent of radiation encountered is not great except under unusual conditions. In an unpublished study Yaglou found that in ordinary frame or masonry dwellings and office buildings heated to from 69 to 75 F. by hot water or steam the radiation effect was approximately equivalent to from -1.6 to $+2$ degrees F. in dry-bulb temperature on the unheated globe and from -2.1 to $+2.5$ degrees F. on the heated globe. These readings were made in the center of the rooms 3 feet above the floor, and the air movement in all instances was less than 40 feet per minute. The rooms had from one to three exposures and the outdoor temperatures during the observations were between 6 and 35 F.

Other readings taken 6 inches from a single-glass window on a cloudy day when the outside temperature was 21 F. showed a cooling effect equivalent to 2.6 degrees F. on the unheated globe and 4.2 degrees F. on the heated globe. Under approximately identical conditions but with the sun shining through the glass the maximum heating effect was approximately equivalent to 34 F. on both globes.

An ordinary thermometer exposed to the same conditions showed a temperature only about 9 degrees F. above air temperature.

Vernon²⁸ reported a similar experience in British factories and homes. The extent of radiation ordinarily experienced there was on the order of \pm or

-1.5 degrees F. on the unheated globe, except in front of furnaces or gas or coal fires, which raised the globe thermometer reading as much as 75 degrees F. above air temperature.

THE EFFECTIVE TEMPERATURE INDEX OF WARMTH

The term "effective temperature"²⁹ is a misnomer because the entity itself is not a "temperature" but a composite index of the degree of warmth resulting from exposure to different combinations of air temperature, humidity and air movement. A more fitting term would be "warmth index." This index was experimentally determined from the subjective sensations of trained men who compared not the relative comfort but the relative warmth of various air conditions in two adjoining rooms by passing alternately from one room to the other. It comprises two different scales: the "basic"^{29a} for men stripped to the waist, and the "normal"^{29c} for men normally clothed (fig. 7).

Air conditions having the same effective temperature index are not necessarily equally comfortable, since warmth is not the only criterion of comfort. High humidity may create discomfort from damp skin and clothing; low humidity may

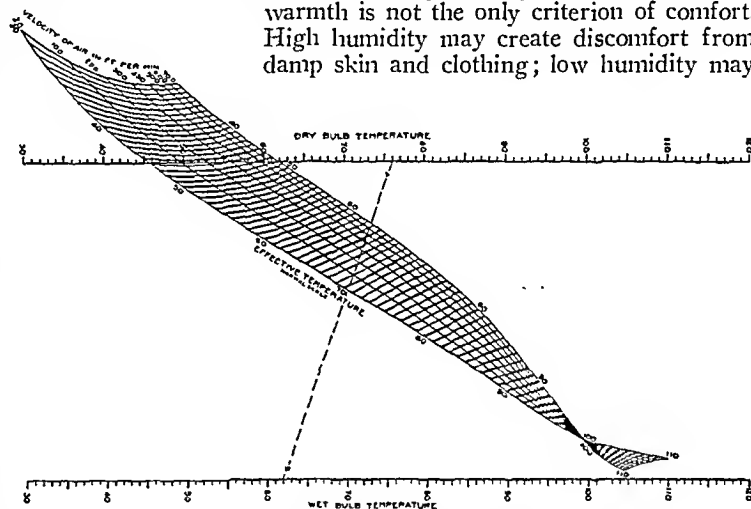


Fig. 7.—Normal scale of effective temperature applicable to inhabitants of the United States wearing customary clothing, at rest or doing light physical work, and in rooms heated by convection methods (Yaglou, C. P., and others: How to Use the Effective Temperature Index and Comfort Charts, Heating, Piping & Air Conditioning 4: 433 [June] 1932).

dry up the skin, eyes or nasal passages. Excessive air movement may be annoying although it may not be actually chilling. Radiation, which is not included in the effective temperature index, not only affects the warmth sensation but may also be responsible for the decided discomfort brought about by simultaneous sensations of heat and cold when different parts of the body are exposed to surrounding surfaces whose temperatures are much above or below that of the body. However, until a better index is introduced, the effective temperature probably will remain the best single index of warmth and the physiologic reactions induced by excessive heat or cold, including humidity effects.

By definition, the effective temperature index of any given combination of air temperature, humidity and air movement is numerically the same as the temperature of still air (velocity under 25 feet per minute) satu-

26. Dufton, A. F.: The Use of Katathermometers for the Measurement of Equivalent Temperature, *J. Hyg.* 33: 349 (Aug.) and 474 (Nov.) 1933.

27. Willard, A. C.; Kratz, A. P., and Fahnstock, M. K.: The Application of the Eupatheoscope for Measuring the Performance of Direct Radiators and Convectors in Terms of Equivalent Temperature, *Heating, Piping & Air Conditioning* 5: 369 (July) 1933.

28. Vernon, H. M.: The Radiation Experienced in Factories and Houses, *J. Indust. Hyg. & Toxicol.* 10: 498 (Nov.) 1937.

29. (a) Houghton, F. C., and Yaglou, C. P.: Determining Lines of Equal Comfort, *Tr. Am. Soc. Heat. & Vent. Engrs.* 20: 163, 1923; (b) Cooling Effect on Human Beings Produced by Various Air Velocities, *ibid.* 30: 193, 1924. (c) Yaglou, C. P., and Miller, W. E.: Effective Temperature with Clothing, *ibid.* 31: 69, 1925. (d) Houghton, F. C.; Teague, W. W., and Miller, W. E.: Effective Temperature for Persons Lightly Clothed and Working in Still Air, *ibid.* 32: 315, 1926.

rated with moisture (100 per cent relative humidity) that will induce the same sensation of warmth as the given air condition. The effective temperature index cannot be measured directly by physical instruments except within a limited range. It is determined from readings of the dry-bulb and wet-bulb thermometers and the velocity of air movement by the use of empirically constructed tables or charts (fig. 7).

The effective temperature index is extensively used in this country, while in England the katathermometer had been in wide use as an index of warmth until it was recently superseded by the eupatheoscope and Vernon's globe thermometer.

One disadvantage of the effective temperature index is that it does not fully allow for radiation effects, since it was determined in rooms heated by convection methods with walls and air at approximately the same temperature. Houghten and McDermott³⁰ attempted to derive correction factors for negative radiation to cold walls, but their experimental conditions were too artificial and the results are not in agreement with those of Bedford³¹ and Winslow and his associates.³²

Missenard³³ has devised a scale of "resultant temperature" based on the effective temperature index but including the effect of radiation. This scale as first used was what might be termed a "synthetic" scale with an arbitrary "fictitious air velocity" which included certain radiation effects as well as true air velocity; the resulting troublesome computations led Missenard³⁴ to develop a "resultant thermometer," which is simply a small globe thermometer $3\frac{1}{2}$ inches in diameter with about one third of its area covered with moist gauze. Experience with this instrument is limited. Bedford states that its indications are not reliable if the air velocity exceeds 40 feet per minute, in which case the resultant temperature must be computed by Missenard's original equation or by means of a chart, later devised, combining individual measurements of the four variables air temperature, humidity, air movement and mean radiant temperature of the surroundings.

A provisional scale of "equivalent warmth" has been constructed and presented in the form of an alignment chart by Bedford³⁵ which is designed to make allowance for radiation effects but is similar to the effective temperature scale developed in this country in that the standard or reference conditions are those of a thermally uniform enclosure in which the air and surroundings are at the same temperature and in which the air is saturated with moisture and is "perfectly still."

BAROMETRIC PRESSURE

The pressure of the atmosphere is not, of itself, an important consideration in ordinary air conditioning. Under abnormal conditions of air pressure special problems do arise such as illness due to compressed air in caisson work and deep sea diving, or symptoms of oxygen deficiency at high altitudes and in airplanes

without airtight cabins, but discussion of such problems is not required in the present report.

Indirectly, barometric pressure may become important through its effect on temperature and humidity as, for example, in underground work at depths of several thousand feet. As one descends the shaft of a deep mine it is usually noted that the air temperature, and in some cases the content of moisture of the air, gradually increases. The temperature increase is due largely to autocompression of the air and to the geothermal gradient of rocks. In the presence of water, part of this heat is consumed in evaporating moisture and the amounts of heat and moisture present set the limit of depth for economic underground operations.

Instruments for measuring barometric pressure are well known and require no discussion here.

ATMOSPHERIC CONTAMINATION

Where indicated, instrumental determinations may be made of air purity with regard to dusts, fumes, vapors, gases, bacteria, pollen or offensive odors not only to discover the nature and quantity of the impurities but also to aid in the selection of an effective and specific method of eliminating undesirable contaminants, whether by direct removal or by displacing the impure air with clean air.

Many types of instruments have been developed for determining the quantity, size and composition of particulate matter in the atmosphere, for detecting the presence of toxic or combustible gases or vapors, or for analyzing the air for its oxygen and carbon dioxide contents. A general discussion of suitable methods and apparatus will be found in the yearbook of the American Public Health Association, which is revised annually.

COMMENT AND SUMMARY

Reliance on ordinary dry-bulb thermometer readings is little warranted as an index of comfort-providing qualities of the air. The use of other instruments is particularly desirable in connection with artificial atmospheres subject to some degree of variation. No single instrument at this time adequately records the thermal quality of the environment combining the four principal factors, namely air temperature, humidity, air movement and radiation. A fair degree of success has attended the development of instruments for combining radiation and convection effects during the heating season, but considerable difficulty has been experienced in attempts to extend the range of these measurements to summer conditions. This difficulty obviously is due to complex physiologic reactions whereby cutaneous blood circulation, rate of perspiration and extent of wetted body surfaces are altered by the body in self defense on exposure to warm conditions. No physical meter can be expected fully to simulate these delicate responses. At the present time "effective temperature" probably is the best index of environmental warmth available. Effective temperature adequately serves with respect to high temperatures and humidities, but since it does not embrace radiation effects its usefulness in determining winter comfort is restricted.

This report, which includes descriptions of many instruments and indexes designed for the measurement or evaluation of air conditions, advocates the use of each instrument or index under those environmental conditions for which it is best adapted.

10 Peterboro Street.

30. Houghten, F. C., and McDermott, P.: Cold Walls and Their Relation to the Feeling of Warmth, Heating, Piping & Air Conditioning 5: 53 (Jan.) 1933.

31. Bedford, T.: The Warmth Factor in Comfort at Work, Report 76, Brit. Indust. Health Res. Board, London, H. M. Stationery Office, 1936.

32. Herrington, L. P., Winslow, C. E. A., and Gagge, A. P.: The Relative Influence of Radiation and Convection upon Vasomotor Temperature Regulation, *Am. J. Physiol.* 120: 133 (Sept.) 1937.

33. Missenard, F. A.: Étude physiologique et technique de la ventilation, Paris, Librairie de l'enseignement technique, 1934.

34. Missenard, F. A.: Théorie simplifiée du thermomètre résultant: Thermostat résultant, Chauffage et ventilation 12: 47, 1935. Bedford, T.: Requirements for Satisfactory Ventilation and Heating, *The Human Factor*, J. Nat. Inst. Indust. Psychol., London 10: 245 (July-Aug.) 1936.

35. Bedford, T.: Warmth and Comfort, *J. Inst. Heat & Vent. Engrs.* 4: 383 (Nov.) 1936; footnote 31.

Council on Physical Therapy

THE COUNCIL ON PHYSICAL THERAPY HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORT.

HOWARD A. CARTER, Secretary.

DENVER RADIOACTIVE PRODUCTS NOT ACCEPTABLE

Manufacturer: Denver Radium Service Laboratories, Majestic Building, Denver.

The Denver Radium Service Laboratories have submitted for consideration by the Council several products containing radium or radon. These products include:

1. One radium emanation jar, called "the vitalizer."
2. Two ampules of radium chloride solution for intravenous injection said to contain from 2 to 50 micrograms of radium chloride 98 per cent pure, in isotonic solution.
3. One ounce of sterile saline solution containing 10 micrograms of radium chloride, for oral administration.
4. One bottle containing 100 tablets, each tablet claimed to contain approximately 10 micrograms of radium chloride with sugar milk base, for oral administration ("Chloradium solution tablets").
5. One bottle (containing 100 tablets) of so-called endocrine compound No. 1 (for male). These tablets are claimed to contain $\frac{1}{20}$ gram of anterior pituitary, $\frac{1}{4}$ gram of suprarenal cortex, $\frac{1}{20}$ gram of thyroid, $\frac{1}{2}$ gram orchic, sugar milk and starch binder. Each tablet is also claimed to contain $\frac{1}{10}$ microgram of radium chloride.
6. One bottle (containing 100 tablets) of endocrine extract No. 2 (female). Each tablet is said to contain $\frac{1}{20}$ gram of anterior pituitary, $\frac{1}{4}$ gram of suprarenal cortex, $\frac{1}{20}$ gram of thyroid, $\frac{1}{2}$ gram of ovarian, sugar milk and starch binder and flavoring. Each tablet is also claimed to contain $\frac{1}{10}$ microgram of radium chloride.
7. One carton of so-called emanation bath (quantity perhaps 2 ounces, but unspecified) and said to contain epsom salt, sodium chloride and 1 microgram of radium chloride.
8. One tube (quantity unspecified) of vaginal jelly, claimed to contain glycerin, gum tragacanth base, lactic acid, quinine hydrochloride, boric acid resorcinol, and $\frac{1}{10}$ microgram of radium chloride per ounce.
9. One carton of so-called vaginal douche (quantity unspecified, but about 2 ounces) claimed to contain alum, menthol, sodium chloride, sodium bicarbonate, tannic acid and epsom salt. The quantity of radium chloride, if any, is not mentioned.
10. One carton of so-called colonic irrigation (rectal) claimed to contain sodium chloride, tannic acid and castile soap. The quantity of radium chloride, if any, is not specified.
11. One bottle ($\frac{1}{2}$ ounce) of ophthalmic solution claimed to be a saline solution containing $\frac{1}{2}$ gram of ephedrine hydrochloride and $\frac{1}{2}$ microgram of radium chloride.
12. One box of urethral bougies (twelve) claimed to contain glycerin, triple distilled water, cocoa butter, gelatin, boric acid, eucrophon, thymol iodide, sulfonal, and $\frac{1}{10}$ microgram of radium chloride.
13. One box (twelve) of vaginal suppositories ("Chloradium suppositories") claimed to contain cocoa butter base, lactic acid, boric acid, resorcinol, zinc iodide and $\frac{1}{10}$ microgram of radium chloride.
14. One box (twelve) of suppositories. This box, which is plainly labeled "rectal," does not contain rectal suppositories but contains what are undoubtedly vaginal ampules made of stiff gelatin, and possibly correspond to the item listed as special vaginal ampules containing gelatin, glycerin, alaterium (?), calcium chloride and $\frac{1}{10}$ microgram of radium chloride.
15. (a) One box containing twelve rectal suppositories wrapped in tinfoil.
(b) One box containing twelve rectal suppositories wrapped in tinfoil.

These two boxes have no outside description to indicate what the suppositories in the two boxes are made of. In the list

furnished by the Denver Radium Service these suppositories are claimed to contain cocoa butter (base), boric acid, anesthesisin, ephedrine hydrochloride and Canada balsam; also each suppository is claimed to contain $\frac{1}{10}$ microgram of radium chloride.

16. One jar (quantity unspecified) of ointment designated as "Narada Balm" and claimed to contain a neutral base, camphor, menthol, 1 gram of eucalyptol oil and 10 micrograms of radium chloride per pound.

17. One jar (quantity unspecified) of chloradium ointment. This is an ointment which, the Denver Radium Service states, can be prepared in any strength of radium chloride from 2 to 50 micrograms per ounce. The charge of 20 cents per microgram for additional radium chloride is made. This ointment is also prepared in tubes with applicator or in opal or glass jars.

The active agent in these products is claimed by the Denver Radium Service to be "Radium" and "the therapeutic value of radium is due to its radioactivity." In the booklet "Therapeutic Use of Radium Emanation Preparations," the firm states that "Radium Emanation is not a drug in the common meaning but a physical agent. It forms no chemical compounds in the body." Since these products are said to be in the category of physical agents, the Council on Physical Therapy has given consideration to them.

Item 1. The "Radium Vitalizer Generator" consists of a chinaware jar $2\frac{7}{8}$ inches in diameter and $5\frac{1}{2}$ inches tall with a small perforated projection at the upper end whereby the vitalizer may be suspended. The middle two thirds of this jar is characterized by multiple perforations about one-eighth inch in diameter arranged in vertical as well as horizontal rows all around the jar. In the bottom of the jar is an opening filled with wax. This opening apparently is the only means of entrance to the interior of the jar, in which is housed a hollow container the nature of which cannot be made out without removing the seal. This container, however, is also perforated and contains fragments of some material made up of irregular pieces of chalk-like substance. In a separate box came a piece of chalk-like material measuring 4.9 by 1.4 by 1 cm. This particular item was not listed in any of the lists prepared and submitted by the Denver Radium Service Laboratories. The method of using the vitalizer is described in a circular. Apparently the vitalizer comes in two forms, a large form for office, hotel or home, and the smaller form for use while one is traveling. This device is described as "a scientifically prepared general purpose device, designed to generate Radium-Emanation in drinking water with distinct therapeutic value." In another paragraph is found the following statement in double face type: "We guarantee the Radium-Active Vitalizer Generating Unit to come within the present requirements of the American Medical Association as to Radium Emanation yield." Another statement is the following: "The Radium-Active Vitalizer is the result of extensive research on the part of the personnel of the Denver Radium Service Laboratories, and other radium authorities who were associated." The method of using the vitalizer is described as follows: "Place the unit in the jar and fill with water. Allow to stand about two hours in order to thoroughly cleanse the unit. Refill the vessel (contents 6 quarts) and allow to stand from 12 to 24 hours in order to become thoroughly activated. Then drink the water as desired, average quantity being 6 to 8 glasses per day. Replace the water consumed during the day, and thus a continuous supply of Radioactive water is assured."

From the foregoing, therefore, the unit within the jar contains the radioactive substance designed to impregnate the water with radium emanation. Tests showed very slight radioactivity when the generator was soaked in 200 cc. of water for forty hours and 60 cc. of this water was used for the determination. Measurements of the radioactivity of the contents of the jar as well as of the separate cake of chalk-like material are given in the accompanying table.

A reliable investigator tested the radioactivity of these products with the following instruments:

(a) *Electroscope*.—An aluminum leaf electroscope connected to an ionization chamber of approximately 300 cc. volume was used. The preparation being tested was placed on top of the ionization chamber and the time of fall of the leaf over a definite part of the scale was determined. The radium content of the

preparation was determined by comparing the rate of fall of the leaf produced by the preparation with the rate of fall produced by the standard after both rates had been corrected for the natural leak of the instrument. A determination was made of the natural leak at least once, the rate for the standard generally twice, and the rate for two or three of the preparations during each half day when measurements were made. The top of the ionization chamber was a piece of aluminum 5 mm. thick which would absorb practically all of the beta radiation. The results may be duplicated with this instrument to within ± 5 per cent.

(b) *Geiger Counter*.—A Cenco Impulse counter was used which would respond to gamma rays but to very few beta particles. The distance of the preparations and the standard from the counter during the tests was varied according to the strength of the preparation so that the number of discharges would be markedly greater than the blank reading (owing to cosmic radiation and unknown radioactive sources) and not too great for accurate counting. A blank reading, a reading for the standard

Measurements on Radioactive Material from Denver Radium Service

No.	Description	Micrograms of Radium Claimed	Micrograms of Radium Measured	
			Electroscope	Geiger Counter
1-A	Radium Vitalizer	25*	7.5	12.3
1-B	Radium Vitalizer sealed in a beaker containing 300 cc. distilled water for 115 hrs. Following tests made on 130 cc. of this water sealed in a flask			
	4 hours after removal from Vitalizer..	..	1.2	2.6
	28 hours after removal from Vitalizer..	..	1.1	...
	52 hours after removal from Vitalizer..	..	0.9	1.6
8-A	Ampule of Ra Cl ₂ Intravenous solution..	20	22.2	23.5
8-B	Ampule of Ra Cl ₂ Intravenous solution..	40	39.2	38.7
6	White Brick, 5 by 1.5 by 0.8 cm.....	10	7.3	8.5
4	1 ounce bottle of Internal Solution.....	10	6.2	6.2
12	Small bottle of Ophthalmic Solution.....	0.5*	0.6	0.5
2	Bottle of 100 Endocrine Compound No. 1 tablets	10	1.2	1.5
7	Bottle of 100 Endocrine Compound No. 2 tablets	10	4.3	6.2
5	Bottle of 100 Internal Solution Tablets...	10	6.0	6.5
3	12 Vaginal Suppositories.....	1.2*	2.3	3.0
9	12 Vaginal Suppositories.....	1.2*	0.1	0.6
10	12 Vaginal or Rectal Suppositories.....	1.2*	0.7	1.1
11	12 Rectal Suppositories.....	1.2*	0.5	1.5
13	15 Urethral Bougies.....	1.5*	1.2	1.9
14	1 Tube of Vaginal Jelly.....	0.15*	0.5	1.6
15	1 Jar of Surgical Dressing.....	3*	0.3	0.9
19	1 Jar of Balm.....	3*	0.5	1.3
16	1 Carton of Bath Salts.....	1*	0.3	1.2
17	1 Carton of Vaginal Douche Salts.....	?	0.3	0.7
18	1 Carton of Colonic Irrigation Salts.....	?	0.1	Trace

* Value obtained from letters or literature and may or may not apply to preparations supplied. In some cases it is not clear whether radium content applies to a single piece or to box; in others radium content is given for an amount of the substance but the amount in the container is not stated. Some preparations are said to be prepared with any amount of radium.

and readings for from one to three of the preparations for one minute each were taken successively until a total of ten readings for each had been made, the results of which may be duplicated with this instrument to within ± 15 per cent.

For a standard of radioactivity a 2 cc. ampule of radium chloride solution, containing approximately 10 micrograms of radium, was used. The accuracy of the solution does not differ from 10 micrograms more than a few per cent. The results are given in the table.

Advertising Material.—The advertising material submitted to the Council with the foregoing items consisted of a pamphlet entitled "Radium Therapeutics and methods of administration for the general practitioner" and eighteen circulars, three of which refer to the use of the radioactive waters in general and the use of the Vitalizer Generator in particular. One of these is a small pamphlet entitled "Radioactive Waters Past and Present." Another contains a description of the Vitalizer Generator and a third circular is a reprint of a sort of list of

the natural sources of radioactivity in natural waters, reprinted from the *Rocky Mountain Druggist*, entitled "Radioactive Waters Past and Present, Extracts from Government Bulletin and Remarks from Authorities." The other circulars refer to the various other preparations prepared and distributed by the Denver Radium Service Laboratories.

One circular entitled "Do you Suffer with . . . Glandular weakness, general debility, muscular exhaustion, irritability, extreme nervousness, loss of weight, insomnia, despondency, stomach and intestinal disorders, chronic constipation, no ambition, poor vital forces" was presented. Then, apparently because this list is not complete enough, a little lower the word "neurasthenia" is brought in. The circular is worded in such a way that the reader is led to believe that any one suffering from any of the conditions mentioned can have these difficulties removed by using "Radiotone Tablets," the radium tablet apparently corresponding to the endocrine tablets listed at the beginning of this report. Stress is laid on the fact that Radiotone Tablets "contain all the different important gland substances and enzymes, in addition to the radium" which is to supply the vitalizing urge. The second circular is headed "Narada Radium Preparations—Why Suffer?" "Used successfully in the treatment of such conditions as rheumatism, neuralgia, arthritis, neuritis, anemia, high blood pressure, gout, neurasthenia, prostatitis, nervous trouble, vaginal trouble, hemorrhoids, and piles."

In a separate one page leaflet entitled "Does Radioactivity Really Benefit? Study this Chart and See" there is given a long list of physical disorders beginning with old age, anemia and asthma and ending with polyarthritis, rheumatism, sciatica and tabes dorsalis, the entire list comprising thirty-one states of physical disintegration, and against each one is given a number of cases supposed to be cured or benefited, as well as a final column containing the supposed number of cases not benefited by treatment with radioactive substances which are not specified, but the impression is given that the treatment was with the Vitalizer Radium Water Jar. Of 111 cases of anemia, for example, seventy-one cases were supposed to have been cured and forty benefited; of 1,291 cases of arthritis, 906 are listed as cured, 219 as benefited and 166 as not benefited. Of 197 cases of chronic metritis, no cases are included in the column of cured cases, 127 in the column of cases benefited and seventy among the cases not benefited. This list is said to have been compiled by Dr. Sigmund Saubermann of Berlin, Germany.

In the case of the products of the Denver Radium Service Laboratories, the amount of radioactive substance contained in any of them is so small that the use of these preparations would probably do no harm, but for the same reason they could not be expected to do any good. If they should be used in larger doses or if their use should be continued for a long time, the possibility of danger cannot be avoided. As the result of repeated experiments on animals as well as clinical observation in human beings, it is now well known that the internal administration of radium or products of radium in certain doses can produce damage to the tissues. When taken by mouth, in excessive doses, these substances are excreted chiefly through the intestine and through the kidneys. Because these substances do not stay long enough in the small intestine they do not produce any lesions there, but in the large intestine, where they stay for a longer time, they produce a hemorrhagic form of inflammation characterized by multiple discrete or massively coalescing petechial hemorrhages, with desquamation, edema and the like. In the kidneys they produce, first, degeneration of the epithelium of the convoluted tubules, followed by edema and more or less intense reactive inflammation.

When substances of this kind are injected intravenously in sufficient doses, not only do the large intestine and the kidneys show lesions similar to those described but corresponding lesions of the liver have been repeatedly described as having occurred in experimental animals.

All of this, therefore, can be summed up briefly as follows: If these substances are used in moderate doses, they can probably do no harm but could also do no good. Considering these points, as well as the character of the advertising literature submitted, the Council cannot very well take any other action than to reject all these preparations as well as all the claims made for them and to make such rejection known to the medical profession.

Council on Pharmacy and Chemistry

REPORT OF THE COUNCIL

THE COUNCIL RECENTLY CONSIDERED THE REPORT OF THE REFEREE ON SULFUR PREPARATIONS ON THE SUBJECT OF COLLOIDAL SULFUR IN THE TREATMENT OF ARTHRITIS. THE REFEREE EXPRESSED THE OPINION THAT NO FORM OF SULFUR SHOULD BE ACCEPTED BY THE COUNCIL FOR THE TREATMENT OF ARTHRITIS UNTIL THERE IS SATISFACTORY EVIDENCE OF ITS USEFULNESS. HE POINTED OUT THAT SATISFACTORY EVIDENCE REQUIRES CONSIDERATION OF THE FOLLOWING FACTORS: THE USE WITH SUFFICIENT CONTROLS AND FOLLOW-UP PERIODS OF OBSERVATION TO RULE OUT SO-CALLED SPONTANEOUS REMISSIONS; THE DETERMINATION OF THE TYPES OF CASES IN WHICH IT MAY BE USED WITH A FAIR EXPECTATION OF BENEFIT; THE DETERMINATION OF THE CHIEF CONTRAINDICATIONS; THE DETERMINATION OF THE OPTIMUM DOSAGE; THE DETERMINATION OF THE BEST FORM IN WHICH SULFUR IS TO BE USED, WHETHER AS FOOD OR AS COLLOIDAL SULFUR, AS ORDINARY SULFUR ADMINISTERED ORALLY, OR AS COLLOIDAL SULFUR FOR INTRAMUSCULAR OR INTRAVENOUS INJECTION.

THE COUNCIL CONCURRED IN THE REFEREE'S CONCLUSIONS AND VOTED TO ACCEPT NO FORM OF SULFUR FOR THE TREATMENT OF ARTHRITIS UNLESS OR UNTIL THE CONDITIONS OUTLINED HAVE BEEN FULFILLED, AND AUTHORIZED PUBLICATION OF THE FOLLOWING REPORT.

PAUL NICHOLAS LEECH, Secretary.

COLLOIDAL SULFUR IN THE TREATMENT OF CHRONIC ARTHRITIS

Osteo-arthritis is the most ancient disease of which there is a record, according to Dr. Joseph L. Miller¹ (1936), who states, however, that not one instance of rheumatoid arthritis of the extremities was noted during the examination of 35,000 Egyptian mummies. Today chronic arthritis and related conditions cause more frequent, intense and lasting pain than any other disease of humanity. Formerly the despair of physicians, it is now studied intensively in clinics at New York, Chicago, Philadelphia, Boston, Rochester (Minn.), New Haven (Conn.), Cleveland, St. Louis, Ann Arbor (Mich.), San Francisco, Tucson (Ariz.) and elsewhere, and progress is being made in the treatment of this condition.

A recent survey made in Massachusetts indicates that there are more than 3,600,000 sufferers from chronic rheumatism² in the United States but that the prevalence varies widely in different regions.

In spite of the enormous numbers of sufferers from arthritis, and its economic importance, there are few conditions which present so many medical problems and concerning which there is such diversity of opinion, especially with reference to therapeutic measures. Attention is often directed primarily to the joints affected, but Pemberton³ (1930) states that atrophic arthritis is a systemic disease and that it is no more a disease of the joints [alone] than typhoid fever is a disease of Peyer's patches. The date of each paper cited is given because the present value of a contribution depends much on the date in this rapidly changing subject.

Sulfur has been used in a host of conditions for centuries and it is natural that it has been used in arthritis. H. E. Miller⁴ (1935) states that colloidal sulfur was first prepared by Debus in 1888. Bory⁵ (1907) and Fleig⁶ (1907) injected it in a variety of conditions, including tuberculosis and syphilis, but their papers do not require further consideration here.

Cawadias⁷ (1917) injected colloidal sulfur intravenously and intramuscularly in subacute rheumatism, in which he claimed that it caused the rapid and complete cessation of pain, retrocession of deformities and restoration of joint functions; the therapeutic effects being alike in the two methods of administration, but the intramuscular injection was not followed by such severe reactions as those after intravenous injection. Patients suffering with subacute and chronic rheumatism lost much incompletely oxidized sulfur.

Comrie⁸ (1917) discussed "trench rheumatism" and allied conditions and stated that the intramuscular injection of colloidal

sulfur, combined with rest and massage, was of the greatest value in subacute painful conditions in muscle and joints; that it was helpful in lingering gonorrheal rheumatism, but that it does not replace salicylates in acute articular rheumatism.

Meyer-Bisch and Basch⁹ (1921) reported that the parenteral administration of sulfur caused increased destruction of albumin with an increase of the sulfur and nitrogen of the urine, the amount of sulfur excreted being much greater than that injected, and that the sodium chloride of the urine was increased transiently, while it, with water, was decreased after two days, at which time there were urobilinuria and glycuronuria. They reported a great difference between the effects of the oral administration of sulfur and that administered parenterally and stated that their results do not explain the clinical effects of the sulfur injected.

Heubner and Meyer-Bisch¹⁰ (1921) reported that after the injection of sulfur in arthritis the sulfate esters of the serum were increased in the stage of fever and that the joint exudates yielded slightly more of these esters than the blood plasma and much more than in two other pathologic exudates, showing that these esters originate only in part from the circulation directly, partly from the walls of the joints. They concluded that this furnishes a basis for the curative value of sulfur in arthritis. Meyer-Bisch¹¹ (1921, 1922) published two papers under the same title: "Ueber die Behandlung chronisch deformierender Gelenkerkrankungen mit Schwefel." He stated that with the onset of fever there was usually less pain in the joints and increased motility. He reported only a few cases, and his paper is of little value now, though his work and that of his associates gave an impetus to the use of sulfur in arthritis.

Rohde¹² (1922), impressed with the work of Meyer-Bisch, also reported favorable results in the treatment of five cases of chronic joint rheumatism with injections of sulfur. There were severe reactions with headache and fever, but so great was the relief that he felt justified in continuing the treatment.

Reimann and Pucher¹³ (1924) expressed doubt that sulfur has any specific action in arthritis deformans, since only those who showed no organic obstruction to joint movements were affected favorably by it. They observed effects very similar to those induced by the injection of nonspecific proteins, and they stated that milk, vaccines and other proteins induce less severe reactions than does sulfur. The intramuscular injection of sulfur in large doses sometimes causes necrosis and acute inflammatory exudate extending far beyond the seat of injection. They tabulated the results in seventeen cases, of which only four showed marked improvement, while nine either failed to improve or were made worse. They were unable to confirm the chemical data of Meyer-Bisch and imply doubt whether the patients of Meyer-Bisch who improved had arthritis deformans.

Vogel¹⁴ (1924) reported a case of sulfhemoglobinemia due to the ingestion of sulfur while the patient was exposed to the action of paraminophenol made by the electrolysis of nitrobenzene. Nitto¹⁵ (1934) observed severe symptoms, including vomiting and diarrhea, in three patients following the percutaneous inunction of purethan (an organic sulfur compound in olive oil for the treatment of scabies). In one of the patients the temperature reached 39.7 C. (97.5 F.), with slight edema about the eyes. The importance of these two reports of toxic actions is due to the fact that the literature contains little regarding the contraindications to the use of colloidal sulfur. One author goes so far as to state that there are no contraindications.

Cawadias¹⁶ (1925) stated that patients suffering with rheumatoid arthritis excrete twice as much sulfur in the urine as normal persons independently of the diet, but he said that there is no increase in the nitrogen eliminated (compare Meyer-

1. Miller, J. L.: Critical Review of Literature on Chronic Rheumatism, Arch. Int. Med. 57: 213 (Jan.) 1936.

2. Until comparatively recently there has been great confusion in the terminology of arthritis and there is still some want of harmony; the terminology in this report is that used by the author cited.

3. Pemberton, Ralph: Arthritis and Rheumatoid Conditions: Their Nature and Treatment, Philadelphia, Lea & Febiger, 1930.

4. Miller, H. E.: Colloidal Sulfur in Dermatology, Arch. Dermat. & Syph. 31: 516 (April) 1935.

5. Bory, L.: Compt. rend. Soc. de biol. 12: 512, 1907.

6. Fleig, C.: Compt. rend. Soc. de biol. 12: 625, 1907.

7. Cawadias, A.: Therapeutic Action of Colloidal Sulfur, Bull. Acad. de méd., Paris 78: 329 (Sept. 25) 1917.

8. Comrie, J. D.: Trench Rheumatism, Lancet 1: 991 (June 30) 1917.

9. Meyer-Bisch, R., and Basch, E.: Biochem. Ztschr. 118: 39, 1921. 10. Heubner, W., and Meyer-Bisch, R.: Biochem. Ztschr. 122: 120, 1921.

11. Meyer-Bisch, R.: Sulfur in Arthritis Deformans, Klin. Wchnschr. 1: 575 (March 18) 1922; Treatment of Chronic Arthritis with Sulfur, München. med. Wchnschr. 68: 516 (April 29) 1921.

12. Rohde, E.: Abstr., Klin. Wchnschr., 1922, p. 864.

13. Reimann, H. A., and Pucher, G. W.: Use of Sulfur in Treatment of Arthritis Deformans, Am. J. M. Sc. 168: 77 (July) 1924.

14. Vogel, Karl: Am. J. M. Sc. 168: 89 (July) 1924.

15. Nitto, S.: Poisoning by Sulfur During the Treatment of Scabies, Jap. J. Dermat. & Urol. 38: 434 (Sept.) 1935; abstr., Arch. Dermat. & Syph. 34: 503 (Sept.) 1936.

16. Cawadias, A.: Rheumatoid Arthritis: Its Causation and Treatment, Brit. M. J. 2: 602 (Oct. 3) 1925.

Bisch); he found no increase in the ethereal sulfates, indicating that there is no destruction of cartilage, since chondroitin sulfuric acid is excreted as ethereal sulfate. Cawadias attributed the increased sulfur elimination to a special disturbance of metabolism in which the patient with rheumatoid arthritis has lost the capacity for retaining sulfur in the tissues. This paper (without title) was presented in a symposium on rheumatoid arthritis in which ten authorities participated, but Cawadias was the only one who recommended the use of sulfur. Rolleston mentioned the long continued popularity of sulfur as an intestinal disinfectant, but it is apparent that Rolleston was not impressed favorably with the report of its use in the treatment of arthritis.

Race¹⁷ (1927) referred to a paper of that year by Cawadias and was inclined to accept the view that there is deficient oxidation in arthritis, but he did not agree with Cawadias that there is an excessive sulfur metabolism in arthritis deformans.

Schlesinger¹⁸ (1931) stated that he found the parenteral administration of sulfur of value in the treatment of neuralgias, syphilis and chronic arthritis. He abandoned the use of 1 per cent solution of colloidal sulfur in olive oil because of the pain induced by the injection.

Wheeldon and Main¹⁹ (1933) determined the toxicity of colloidal sulfur in experiments on dogs, rabbits and guinea pigs and stated that it may be used therapeutically without danger. They used healthy animals, presumably; hence their results throw little light on the contraindications due to abnormal conditions.

Cecil²⁰ (1933) said with reference to rheumatoid arthritis: "Drugs can be quickly dismissed. Iron for anemia, arsenic and strychnine for their tonic effects, the salicylates to ease pain—that about covers it." He²¹ discussed the medical treatment of chronic arthritis in 1934, at which time he said "I have been quite disappointed in the results obtained from various forms of sulfur and the various preparations of iodine that have been recommended."

Woldenberg²² (1934, 1935) reported extraordinary success in the treatment of arthritis with colloidal sulfur. These papers will not be reviewed further in this place because of the severe criticism of Hench and others²³ (1936); of the second of these they state (p. 830): "It is difficult indeed to believe these extravagant statements, particularly in view of the more conservative reports of others. The patients received physiotherapy daily. No control series was observed and no details of the follow-up are given." Woldenberg²⁴ (1937) reported that 356 patients had been treated with colloidal sulfur. The later paper is principally a continuation of the first two.

Sullivan and Hess²⁵ (1934) found an average of 11.69 per cent of cystine in the finger nails of twenty-six normal persons and an average of 9.77 per cent in 103 patients suffering with arthritis. They recommended the use of sulfur on the theory that patients with arthritis have some material which reacts injuriously with sulfur. Seven patients were treated with colloidal sulfur by Argy²⁶ (1934), who reported that six showed some clinical improvement with an increase in the cystine content of the nails. He stated that fever was not induced; there was slight extravasation with sloughing in one case.

Klauder and Brown²⁷ (1935) also reported that the sulfur content of the hair and nails was below normal in 91 per cent

of thirty-three patients having various systemic infections, including some with chronic arthritis.

Senturia²⁸ (1934) reported improvement in 75 per cent of sixty unselected patients suffering with arthritis and rheumatoid conditions treated by the intramuscular injection of colloidal sulfur. He reported a total of 1,035 injections. He found no difference in the therapeutic effects of intramuscular and intravenous injections. There was no fever after intravenous injection, but there was an occasional slight rise of temperature after intramuscular injection, and some pain when any of the fluid escaped into the subcutaneous tissue. Senturia states that no other therapeutic measures were used in these cases. He also states that there are no contraindications.

Wheeldon²⁹ (1935) reported the use of colloidal sulfur in the treatment of 892 patients suffering with arthritis. An analysis of this paper would seem unnecessary, especially since it is readily available to those who are interested in the subject.

Krestin³⁰ (1935) reported the results of treatment of fifty patients with chronic nonspecific arthritis with intramuscular injections of sulfur. Eighteen showed good results in thirty cases in which the bony changes were slight or moderate; nine were so classed among fourteen in which there were advanced bony changes or the patients had osteo-arthritis. Krestin states that it is extremely difficult to determine the value of any treatment in chronic arthritis, for, excluding specific conditions, such as gout and gonorrhea, striking improvement occurs spontaneously occasionally or after the most diverse treatment. He discontinued the use of colloidal sulfur as unsatisfactory. He mentions numerous contraindications, including advanced emaciation, feebleness, nervousness, hysteria or psychopathic condition, the presence of organic disease (other than arthritis) and obesity (compare Senturia).

Rawls, Gruskin and Ressa³¹ (1935) reported the results of treatment of 100 patients with sulfur. They reported that fairly large doses of colloidal sulfur (from 10 to 30 mg. twice a week) are usually well tolerated but that larger doses induce toxic symptoms in some cases; these include fatigue, drowsiness, headache, increased pain, stiffness or swelling of the joints, which usually disappeared in five days. They reported that the cystine content of the nails was increased in those cases in which it had been below normal, the improvement being greater in those in which the cystine content had been subnormal. They believed that colloidal sulfur is a valuable agent in the treatment of certain types of arthritis.

Sashin and Spanboch³² (1935) administered an average of 600 mg. (totals) of colloidal sulfur to twenty ambulatory patients. They state: "From our small series of twenty cases, no definite conclusions can be drawn as to the efficacy of colloidal sulfur in the treatment of rheumatoid and osteo-arthritis. This form of therapy deserves further study and observation."

Kinsella³³ (1935) stated that nothing very important had been accomplished in the treatment of some fifty to sixty patients suffering with rheumatoid arthritis in the orthopedic clinic associated with the arthritis clinic of Desloge Hospital but that the mere fact that from seventy-five to 100 injections were given [to each patient] is an indirect argument against the value of the drug.

Forbes and others³⁴ (1936) reported that a majority of patients suffering with chronic arthritis improved on diets which were high in protein and low in carbohydrates; especially was this true of those having the rheumatoid type, and coincident with the improvement indoluria diminished and then disappeared. This suggested that indole is causally related to chronic arthritis and that a diet rich in sulfur is indicated. They suggest that

17. Race, J.: Sulfur Metabolism, *Lancet* 2:142 (July 16) 1927.

18. Schlesinger, H.: Erweiterung der Indikationen für die Schwefeltherapie bei inneren Erkrankungen, *München. med. Wchnschr.* 78:1300 (July 31) 1931.

19. Wheeldon, T. F., and Main, R. J.: Use of Colloidal Sulfur in Treatment of Arthritis, *J. Bone & Joint Surg.* 15:94 (Jan.) 1933.

20. Cecil, R. L.: Rheumatoid Arthritis: New Method of Approach to Disease, *J. A. M. A.* 100:1220 (April 22) 1933.

21. Cecil, R. L.: Medical Treatment of Chronic Arthritis, *J. A. M. A.* 103:1583 (Nov. 24) 1934.

22. Woldenberg, S. C.: Sulfur (Colloidal) Therapy in Treatment of Arthritis, with Report of 100 Cases, *M. Rec.* 139:161 (Feb. 21) 1934; Treatment of Arthritis with Colloidal Sulfur: Report of 250 Cases, *South. M. J.* 28:875 (Oct.) 1935.

23. Hench, P. S., and others: The Problem of Rheumatism and Arthritis: Review of American and English Literature for 1935, *Ann. Int. Med.* 10:754 (Dec.) 1936.

24. Woldenberg, S. C.: Clinical Evaluation of Colloidal Sulfur in Treatment of Arthritis, *J. Bone & Joint Surg.* 19:1003 (Oct.) 1937.

25. Sullivan, M. X., and Hess, W. C.: Cystine Content of Finger Nails in Arthritis, *J. Bone & Joint Surg.* 16:185 (Jan.) 1934.

26. Argy, W. P.: Arthritis: Treatment with Sulfur by Intravenous and Intramuscular Injection, *J. Bone & Joint Surg.* 16:909 (Oct.) 1934.

27. Klauder, J. V., and Brown, Herman: Sulfur Content of Hair and Nails in Abnormal States: Nails, *Arch. Dermat. & Syph.* 31:26 (Jan.) 1935.

28. Senturia, B.: Results of Treatment of Chronic Arthritis with Rheumatoid Conditions with Colloidal Sulfur, *J. Bone & Joint Surg.* 16:119 (Jan.) 1934.

29. Wheeldon, T. F.: Use of Colloidal Sulfur in Treatment of Arthritis, *J. Bone & Joint Surg.* 17:693 (July) 1935.

30. Krestin, David: Treatment of Chronic Nonspecific Arthritis by Intramuscular Injections of Sulfur, *Brit. M. J.* 2:1144 (Dec. 14) 1935.

31. Rawls, W. B.; Gruskin, B. J., and Ressa, A. A.: Value of Colloidal Sulfur in Treatment of Chronic Arthritis, *Am. J. M. Sc.* 150:400 (Sept.) 1935.

32. Sashin, David, and Spanboch, Joseph: Intravenous Injection of Colloidal Sulfur in Treatment of Rheumatoid and Osteo-Arthritis, *Radiol.* 142:332 (Oct. 2) 1935.

33. Kinsella, R. A.: Medical Aspects of Chronic Arthritis, *Radiol.* 24:413 (April) 1935.

34. Forbes, J. C., and others: Studies of Effect of High-Sulfur Low-Carbohydrate Diet in Chronic Arthritis, *J. Lab. & Clin. Med.* 21:1153 (July) 1936.

adoloria may be due to impaired liver function resulting from deficiency of sulfur in the liver. All but six of their thirty-two patients, and all but two of twenty-two who had rheumatoid arthritis, improved markedly, but they were unable to determine whether that improvement was due to sulfur of the diet, to vitamin B or to the low carbohydrate diet.

This paper is cited at some length because of the very fact that while it contributes little or nothing to our knowledge of sulfur therapy it is more or less characteristic of a type of paper dealing with this subject, but it differs from many in its conservative attitude.

Johnson³⁵ (1936) reported that 500 patients having chronic arthritis were treated with sulfur at the Freedmen's Hospital during the years 1930-1935. He presented an analysis of twenty-two cases with complete relief in four, some relief in nine and little or none in four. Five refused to continue the treatment.

Clark³⁶ (1937) treated twenty selected patients suffering with mixed or hypertrophic arthritis, using total amounts of from 360 to 1,060 mg. of colloidal sulfur, the latter dose in a period of three months. He attributes his success to the relatively large doses and states that there was no fever, nausea, loss of appetite or other [undesired] reaction. He stated that he had observed the clinical course of a majority of the 892 cases reported by Wheeldon. Various measures, including diet, iodine, thyroid, salicylate, vaccine, nearsphenamine, cacodylate, vitamin D or potassium iodide [not all for any one patient] had been used before the treatment with sulfur was begun. It is impossible to estimate the value of this paper, since so many measures were employed, and any improvement may have been spontaneous or due to delayed effects of other treatment.

Parmenter³⁷ (1937) reported that sulfur tends to normalize the body metabolism and vitalize cell tissues by supplying sulfur deficiency, shown by its effects on blood pressure, weight and symptomatology. He reported complete relief in 30 per cent of his cases and relief from pain and reduction of swelling of joints in 58 per cent. [See comment of Hench and others concerning various theories of the cause of chronic arthritis.]

Thompson, Wyatt and Hicks³⁸ (1938) presented an analysis of 343 cases of chronic arthritis, with treatment and a follow-up summary of 274, at the Wyatt Clinic and Research Laboratories at Tucson. They enumerate drugs used and state that "sulfur and gold have been disappointing in our experience but we have noted some beneficial effect with massive doses of vitamin D."

It is believed that the foregoing abstracts fairly represent the literature relating to the use of colloidal sulfur in the treatment of chronic arthritis as it is presented by those who have actually employed it in their own practice. The remainder of this review will be devoted mainly to citations of reviews by those best qualified to judge of the merits of the work of others in this field.

Irons³⁹ (1934) did not mention sulfur in his paper on the treatment of chronic arthritis, but he stated: "Any harmless therapeutic measure, whether actually effective or not, will, if instituted in the beginning of a natural remission, be followed by improvement and thus be credited with a value it does not deserve."

Pemberton³ (1930), who is well known for his long continued and intensive studies of arthritis, stated (p. vi): "Many observations and measures of alleged value in arthritis have lacked in the past critical scientific basis." After discussing the work of Cawadiaz and that of Race he says: "On the basis of such findings, injections of various preparations of sulfur have been used extensively in Europe, though apparently less so in this country, but it is not clear that the advantages from their use are other than those which follow nonspecific protein at large, according to the work of Reimann and Pucher. It also appears that considerable soreness may ensue. . . . Perhaps in no other disease have so many drugs been advocated with so little success."

Joseph L. Miller¹ (1936) presented a critical review of the literature of chronic rheumatism. He stated: "Sulfur Therapy. . . . The recent literature contains numerous reports on the curative value of colloidal sulfur administered intramuscularly or intravenously. In none of the reports is mention made of suitable controls having been used or of a careful objective study of the reputed improvement. The period of treatment is prolonged, and this gives an opportunity for spontaneous improvement." Miller quotes Osler as follows: "In treatment the placid faith of the believer, not the fighting faith of the aggressive doubter, is our besetting sin." And Miller adds: "This statement, I believe, may be well applied to the therapy of rheumatoid arthritis in the past. It is the aggressive doubter who insists that the control method be employed." It may be added that many manufacturers must be reminded of this self-evident fact.

Hench and others presented the Third²³ (1936) and Fourth⁴⁰ (1938) Reviews of English and American Literature for the American Rheumatism Association, based on more than 1,100 papers and thirty-two books. Several quotations from these reviews suffice to show that the authors do not consider colloidal sulfur of much importance in the treatment of arthritis. They state that Todd⁴¹ (1935) approved of sulfur therapy but that Dawson⁴² (1935) found sulfur absolutely without [therapeutic] effect in twelve cases.

They²³ state (1936, p. 841) under "Factor of Altered Metabolism": "In contrast to the idea of a nonspecific metabolic defect from poor articular circulation is the theory that some more or less specific metabolic derangement is responsible, a disturbance in the utilization of sugar, of calcium, of sulfur. A defect of the last type is now a popular notion, and some believe that hypertrophic as well as atrophic arthritis is due to a deficiency of sulfur in the body, particularly in cartilage. The majority have made no attempt whatever to differentiate the types of arthritis in which they found reduced cystine in the nails or which improved on sulfur, labeling them "arthritis" or "chronic arthritis." They add: "It is impossible for a critical reader to form any conclusion when even the types of arthritis treated are not differentiated." Elsewhere they stress the value of controls as follows: "Herein, however, lies the difficulty in evaluating researches on treatment, for in most cases the measure used was but a part of a larger plan of treatment, though the writer often fails to mention the fact. *Thus the matter of setting up controls is so difficult, yet so important.*"

The Fourth Report⁴⁰ (1938) differs little from the Third so far as colloidal sulfur is concerned, as the following quotations show. With reference to atrophic arthritis they state: "Lacking a specific remedy, physicians have too often, like the children of Israel, wandered far after strange gods. Although some studies on therapy have been well controlled and have taken into consideration the natural history of arthritis and its tendency to spontaneous remissions, too many have consisted of uncritical observations of a few patients for a short time and are of little value. . . . The trend is away from drugs, since most of them have not justified themselves."

It would seem to be of great significance that not one of the leading arthritis clinics of the United States has adopted the use of sulfur in the treatment of arthritis, so far as can be determined.

Sulfur may have some therapeutic value in affording temporary symptomatic relief in some forms of arthritis, but the literature does not afford evidence concerning the type of cases in which it may be useful. It often induces fever (and other symptoms) but it is not known whether the fever will be useful or harmful in a given case. There is an almost total lack of knowledge concerning the contraindications. The optimum dose has not been determined. It is unsuited for experimental use except in institutions, or under other conditions in which its effects may be followed intelligently and accurately for prolonged periods.

35. Johnson, P. T.: Clin. Med. & Surg. 43: 332, 1936.
36. Clark, M. M.: Clinical Experience with Colloidal Sulfur in Treating Mixed and Hypertrophic Arthritis, New York State J. Med. 37: 569 (March 15) 1937.

37. Parmenter, D. C.: Sulfur Therapy in Arthritis: Preliminary Report of Some Clinical Results, Kentucky M. J. 35: 14 (Jan.) 1937.

38. Thompson, H. E.; Wyatt, B. L., and Hicks, R. A.: Chronic Atrophic Arthritis, Ann. Int. Med. 11: 1792 (April) 1938.

39. Irons, E. E.: Treatment of Chronic Arthritis: General Principles, J. A. M. A. 103: 1579 (Nov. 24) 1934.

40. Hench, P. S., and others: Present Status of Rheumatism and Arthritis: Review of American and English Literature for 1936, Ann. Int. Med. 11: 1089 (Jan.) 1938.

41. Todd, A. T.: System of Treatment of Chronic Rheumatism, Practitioner 135: 692 (Nov.) 1935, cited by Hench and others⁴⁰ (1936).

42. Dawson, M. H.: Nelson's Loose-Leaf Medicine, vol. V, p. 643.

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SATURDAY, OCTOBER 29, 1938

NONMEDICAL FACTORS AFFECT- ING HEALTH

Many factors other than the actual rendering of medical and allied services may affect the maintenance of good health and recovery from disease. Urban or rural residence is important in mortality and morbidity expectation. White infants born in the country today may expect to live about five years longer than white infants born in the city if they are boys and four years longer if they are girls.¹ Typhoid, however, takes relatively more than twice as many lives in rural areas as in cities. Rural residents continue to possess definite advantages over urban residents in health prospects.

Housing is a fundamental consideration in the general health problem. Poor housing is often associated with poverty, ignorance, inadequate food, long hours of toil, hazardous employment, unfavorable climate, unhygienic living and still other factors which have a more direct bearing on health.² While a house itself ordinarily does not have a significant part in regulating or controlling morbidity or mortality rates from communicable diseases, healthful living demands sanitary equipment in the environment. Poor housing influences the health of the occupants directly through the transmission of infection and through the debilitating effects of an unfavorable environment.

Climate is a factor of importance over which we have no control. Recent discussions indicate that climate may influence the nervous system,³ the upper respiratory system⁴ and rheumatic heart disease,⁵ as well as many other conditions.⁶ The importance long attached by some to the climate of spas and resorts is a further indication of its significance.

1. Dorn, H. F.: *The Relative Amount of Ill Health in Rural and Urban Communities*, Pub. Health Rep. 53:1181 (July 15) 1938.
2. Horwood, M. P.: *Housing and Health*, Commonwealth 25:95 (April-May-June) 1938.
3. Critchley, Macdonald: *Climate and the Nervous System*, J. State Medicine 45:98 (Feb.) 1937.
4. Charlton, C. C.: *Climate and the Upper Respiratory System*, Arch. Otolaryng. 26:1 (July) 1937.
5. Paul, J. R., and Dixon, G. L.: *Climate and Rheumatic Heart Disease*, J. A. M. A. 105:2096 (June 19) 1937.
6. Lorenz, F.: *Untersuchungen in der Klimakammer beim gesunden und kranken Menschen*, Ztschr. f. klin. Med. 133:178 (Dec.) 1937.

Disease and quite probably health are also definitely related to hereditary or constitutional factors. The hereditary diseases are too well recognized to require reemphasis; but the role of heredity in cancer,⁷ which now seems to be established, as well as its possible place in the genesis of other less definitely recognized hereditary diseases,⁸ indicates how heredity may affect general health. The importance of diet has been recently reemphasized by McLester,⁹ by Langdon-Brown¹⁰ and by Christiansen,¹¹ who call attention to the relation between nutrition and the health of whole peoples.

The effects of industry and occupation on groups and individuals is also of fundamental consequence. While occupational accidents and hazards of other kinds have received concentrated scrutiny in many industries, the effect of prolonged work under conditions perhaps unfavorable to the nervous system is only beginning to be recognized. No doubt the role which such factors have in the general picture will become clarified in the future. Finally the direct effects of poverty and economic status on the incidence of disease cannot be ignored. Poverty, or at least the deficiencies in environment associated with poverty, are directly related to the incidence of certain disease and subnormal conditions. Only recently factors of this nature have been reported both here and abroad.¹²

The whole problem of improving the health and the average life span of the American people is mingled with factors which the medical profession can regulate only indirectly rather than by the employment of its professional services alone.

VITAMIN C IN THE TONSILS AND BLOOD OF CERTAIN CHILDREN

The theory that deficiency of vitamin C may be a factor associated with rheumatic fever has been supported by clinical, experimental and epidemiologic data.¹ Studies of 107 children with active rheumatic fever in 1936 indicated a greatly increased metabolic use of vitamin C in those who suffer from the infection which underlies rheumatic fever.² Kaiser and Slavin³ have recently studied the incidence of hemolytic streptococci in the tonsils in relation to the amount of

7. Bonne, C.: *Cancer and Human Races*, Am. J. Cancer 20:43 (July) 1937.
8. Richardson, W.: *A Note on Racial Incidence in Portal Cirrhosis*, New England J. Med. 219:257 (Feb. 10) 1938.
9. McLester, J. S.: *The More Abundant Diet*, J. Am. Diet. A. 14:1 (Jan.) 1938.
10. Langdon-Brown, Wyman: *Diet and the National Health*, J. R. Inst. Pub. Health & Hyg. 1:259 (Feb.) 1938.
11. Christiansen, Johanne: *Nutrition and Disease in Denmark*, Lancet 1:336 (Feb. 5) 1938.
12. Reid, W. J. S., and Mackintosh, Jean M.: *The Influence of Anemia and Poor Social Circumstances During Pregnancy on Subsequent History of Mother and Child*, Lancet 2:1389 (Dec. 11) 1937. Pech, Cecilia: *Behavior Problems of Children from High and Low Socioeconomic Groups*, Ment. Hyg. 21:452 (July) 1937.
1. Rinehart, J. F., and Mettler, S. R.: *Heart Valves and Muscles in Experimental Scurvy with Superimposed Infection, with Notes on Etiology of Lesions to Those of Rheumatic Fever*, Am. J. Path. 10:11 (Jan.) 1934.
2. Abbasy, M. A.; Hill, N. G., and Harris, L. J.: *Vitamin C and Juvenile Rheumatism*, Lancet 2:1413 (Dec. 12) 1936.
3. Kaiser, A. D., and Slavin, Betty: *The Incidence of Hemolytic Streptococci in the Tonsils of Children as Related to the Vitamin C Content of Tonsils and Blood*, J. Pediat. 12:322 (Sept.) 1938.

vitamin C in the blood and in the tonsils themselves. One hundred and twenty-three children had been selected by school physicians for tonsillectomy. Five cc. of blood was withdrawn from a vein and a quantitative determination of the content of vitamin C was made the following morning. The tonsils were sent to the laboratory immediately after removal and a quantitative determination of the vitamin C content was made. To determine the presence of streptococci in the tonsils, the surface was seared and cut with a sterile knife; then from the cut surface loops were streaked on blood agar plates. Streptococci thus obtained were subcultured for determination of their virulence. These children were not acutely ill. They came from families on relief or families classed in the lower economic strata. Since ninety-six of the children were under observation for six months or more after tonsillectomy, it was possible to determine also something about the amount of vitamin C in the diet and the incidence of respiratory infections.

The vitamin C content of the blood varied from 0.5 mg. per hundred cubic centimeters to 1.08 mg., while that of the tonsils varied from 18.6 to 53.7 mg. Hemolytic streptococci were demonstrated in about 50 per cent of these children.

There was no constant relation found between the amount of vitamin C in the blood and that in the tonsils. Frequently children whose level of vitamin C in the blood was low showed an average or above average amount of vitamin C in the tonsils and vice versa. In a group of thirty-one children whose vitamin C content of the tonsils was low, 40 per cent of the tonsils showed evidence of hemolytic streptococci, while in a group of thirty children whose vitamin C content of the tonsils was high only 26 per cent of the tonsils showed evidence of hemolytic streptococci. A similar analysis by Kaiser and Slavin shows that in the group presenting the lower third of vitamin C blood values 55 per cent of the tonsils showed evidence of hemolytic streptococci, while in the upper third only 10 per cent of the tonsils showed evidence of streptococcal infection. There was a significant difference also in the percentage of hemolytic streptococci found in the tonsils. Hemolytic streptococci were found five times as often in cases in which the vitamin C blood values were 0.7 mg. per hundred cubic centimeters or less than when the blood values were 0.85 mg. or more. Further analyses of the data were made by mathematical methods which appear to show that the vitamin C content of the blood and of the tonsils is lower in children whose tonsils contain hemolytic streptococci than in those whose tonsils do not contain these organisms.

The significance of finding hemolytic streptococci in the tonsils was not clear, as there were no apparent symptoms present in the majority of children in whom

the organisms were found. Virulence tests showed that 40 per cent of the streptococci in the tonsils of children having the lowest vitamin C values were virulent and that only 10 per cent of the streptococci found in those whose vitamin C values were above the average were virulent.

These results suggest that streptococci are less likely to be found in tonsils when the vitamin C values of the blood are high and that when present in such cases they are seldom virulent. While the vitamin C content of the blood is probably determined by the amount taken in with certain foods, the daily ingestion of a reasonable amount of orange juice apparently does not assure a high level of vitamin C in the blood in all instances. When generous amounts of vitamin C are taken daily in the form of fruit juices, the vitamin C blood levels are uniformly high or are in the average zone. The definite determination that there are fewer streptococci present in the tonsils of children with an average or better vitamin C content suggests an inhibitory relation. The desirability of supplying the children with more than the minimum amount of vitamin C in their diets is obvious.

Current Comment

INCREASE IN FELLOWSHIP DUES AND IN THE SUBSCRIPTION PRICE OF THE JOURNAL

After careful consideration of all factors involved, the Board of Trustees by unanimous vote of its members has decided to increase the annual Fellowship dues and the subscription price of *THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION* to \$8 after Dec. 31, 1938. This decision of the Board of Trustees was taken in accordance with the provisions of the By-Laws of the Association authorizing the Board to fix the annual Fellowship dues and subscription price of *THE JOURNAL* at a sum not in excess of \$8 and to announce the amount in *THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION* not later than November 1 of each year. This action of the Board, whereby the annual Fellowship dues and subscription price of *THE JOURNAL* will be increased by the sum of \$1 beginning Jan. 1, 1939, was made necessary by the constantly expanding work of the Association and by reason of certain contingencies that have arisen which will undoubtedly require some unusual expenditures during the coming year. Annual Fellowship dues and subscription to *THE JOURNAL*, under the provision of the By-Laws, are payable in advance on the first day of January of each year.

"LIFE" AIDS ANIMAL EXPERIMENTATION

Life for October 24 is for American medicine a new and greatly appreciated ally. The benefits which have come to mankind through the use of animals are clearly presented and the advantages of research on animals are shown to the public in a telling pictorial fashion. Thus an issue long hidden from public understanding is now brought clearly before the American people. Perhaps the natural smugness which settles on a comfortable people will be rudely shattered by this exposition of factual data. But the people as a whole must recognize the difficulties which a small but vociferous minority have thrown in the way of medical progress. Each of us must assist in every way possible. Encourage patients to study this issue of *Life*. Amplify the statements for them so that they may comprehend how modern medicine came into existence through investigation on animals. Be prepared to show that the discovery of bacteria as a cause of infectious diseases not only is the basis of modern surgery, which would not exist without a complete understanding of bacteria, but is largely responsible for the extension of life in our day and generation. Tell your patients that other types of disorders have yielded secrets under animal investigation, for example, the use of insulin in the treatment of diabetes and of liver in the treatment of pernicious anemia. Explain the powerful roles assumed by minute quantities of chemical substances known as vitamins and hormones, and indicate that these also have been discovered through animal investigation. Those physicians who must each year hie themselves to the committee rooms of state capitols to protect further scientific endeavor in laboratories for the good of the people will be relieved that such a powerful aid has come to their assistance. Former generations looked on animal investigators as monsters and blasphemed the people who sought to help them. That ancient attitude still prevails in a few places. Remember that the "Humane Pound Law" is to be voted on by the citizens of California on November 8. Public opinion will be formed in the next few weeks. The responsibility for this opinion rests with the medical profession and their biologic colleagues.

DRUGS IN TREATMENT OF ARTHRITIS

Elsewhere in this issue (page 1657) appears a report of the Council on Pharmacy and Chemistry on colloidal sulfur in the treatment of arthritis. This report, based on an extensive review of the literature, points out that studies to date have failed to indicate the type of case in which sulfur may be useful, the contraindications or the optimal dose. The Council concurred in the referee's conclusions and voted not to accept any form of sulfur for the treatment of arthritis at present. The introductory statement affirms that before acceptance satisfactory evidence must be produced that sufficient controls have been employed and that follow-up periods of sufficient length to rule out spontaneous remissions have been observed. Further, the types of cases in which the preparation may be used with a fair expectation of benefit must be deter-

mined, and the chief contraindications, optimal dosage and best form and route for use must be defined. These criteria as outlined for sulfur therapy in arthritis could well be employed in assessing the value of any other of the many drugs employed in this chronic and clinically variable disease. That they have not been so employed, however, is demonstrable by the repeated exploitation of numerous proprietary remedies with extravagant claims as cure-alls for arthritis of all types. While considerable skepticism as to the value of colloidal sulfur in arthritis has previously been expressed elsewhere, this report of the Council should serve to crystallize the objections to accepting this form of therapy as in any way scientifically established. Likewise, the criteria outlined in the introduction are just as applicable to other therapeutic agents employed in this chronic disease or for that matter any other long continued protean disease process. No doubt further uncontrolled favorable reports of drug therapy in arthritis will appear in the literature but subsequent studies on this subject emanating from reliable sources will doubtless pay more attention to the critical evidence required.

RHYTHM IN EPILEPSY

In addition to recording the incidence of epileptic fits in 110 boys and men among the patients in the Lingfield Epileptic Colony over prolonged periods, Griffiths and Fox¹ noted the effects of drugs and other factors on the frequency and time of appearance of the convulsions. Charts were constructed including all major attacks and minor attacks involving loss of consciousness with or without partial convulsion. A study of the charts showed that many patients have fits either singly or in groups at regular intervals. Observation of the time of day of fits showed that many epileptic patients have a predilection for certain hours for their fits. If all fits, both major and minor, of the 110 patients studied (39,929 fits) are assembled, the greatest incidence appears between 6 and 7 a. m., there being a steady rise from 3 a. m. to this peak and an abrupt fall at 8 a. m. The next most popular time for fits was between 5 and 9 p. m. and between 9 and 11 a. m. These investigators also observed the effect of phenobarbital, bromide, borax, chloral and certain other commonly employed drugs on the convulsions. They are able to report a number of cases in which the day was cleared of fits by phenobarbital, bromide, borax or a combination of two of them. The determination of the individual patient's inherent or constitutional time incidence of fits requires a considerable period of observation without any drugs, but, when this method is followed, inherent rhythms both of a "long distance" and a "time of day" type have been found in many cases. Furthermore, in such cases the effective modification of the "time of day" rhythm frees them from the risk of accident and from interference with their daily occupation. While further clinical and biochemical investigations are indicated, this series of observations may well be linked at some future time with the recently reported encephalographic studies of the same disease.

1. Griffiths, G. M., and Fox, J. T.: Rhythm in Epilepsy, *Lancet* 2: 409 (Aug. 20) 1933.

ORGANIZATION SECTION

GRAND JURY INVESTIGATES ORGANIZED MEDICINE.

On October 17 the special grand jury called in the District of Columbia to investigate organized medicine began its study. The attorneys representing the government include John Henry Lewin, a special assistant selected by the Department of Justice, former city solicitor in Baltimore and later the people's counsel to the Maryland Public Service Commission. He is a graduate of Johns Hopkins University and the Harvard Law School. In 1933 he became a member of the trial section of the A. A. A. legal division and in 1937 conducted the government's antitrust case in Madison, Wis., against the oil companies. Mr. Lewin is 40 years old and was for a while editor of the *Harvard Law Review*.

His principal assistant in the case is Allan Hart of Portland, Ore., who first came to the attention of Mr. Thurman Arnold at Yale. In 1926 Mr. Hart was appointed assistant United States District Attorney in Portland and he was taken from that position to assist Mr. Arnold in Washington.

In addition to these two attorneys, the Department of Justice is utilizing Grant W. Kelleher and Douglas B. Maggs, the latter called to the Department of Justice from Duke University specifically for this case.

The first of the witnesses to be called before the grand jury was Dr. Hugh Cabot. It is understood that the attorneys for the Department of Justice wished to keep secret, if possible, the names of witnesses to be called before the grand jury. In interviews with reporters after testifying, Dr. Cabot declined to discuss his testimony but, according to the press, while waiting to be summoned to the grand jury room he discussed his theories of medical service. He deprecated proposals to subsidize treatment in the hands of private practi-

tioners for people unable to afford regular medical charges. Apparently Dr. Cabot indicated his conviction that medicine is not a "trade." He is also reported to have said "Whether a criminal prosecution is the right approach to the problem I cannot say; I am not expert on criminal prosecutions. However, I can say that other methods which have been employed have not been successful; the problem remains unsolved."

The second witness called was Michael M. Davis, who is still called by the newspapers "a leader of the medical profession." Mr. Davis was associated with the Rosenwald Foundation and the Committee on the Costs of Medical Care and is now listed as chairman of the National Committee for Research in Medical Economics—a body which apparently he has organized.

The third witness seems to have been Mr. Charles W. Taussig, president of the American Molasses Company. Mr. Taussig was apparently the only representative of capital to take part in the National Health Conference. He has not been heard of previously in relationship to problems of medical care.

The fourth witness was one Clem Linnenberg, staff economist of the antitrust division of the Department of Justice. Reporters indicate that when he entered the grand jury room he was accompanied by a large chart which was carried by court attendants.

As we go to press there are indications that additional witnesses will be Theodore Wiprud, executive secretary of the Medical Association of the District of Columbia, and William C. Woodward, director of the Bureau of Legal Medicine and Medical Legislation of the American Medical Association.

PROFESSION COMMENDED BY ILLINOIS STATE CONVENTION

At the Republican State Convention in Peoria, Ill., August 31, the following resolution commending the medical profession was unanimously adopted:

The Republican Party commends the medical profession for its fine and sacrificial service rendered mankind. We believe that profession should be protected as an independent force for human good free from political domination or control. The

American doctor has earned the praise and acclaim of the world by his unselfish efforts administering to human ills.

The Republican Party pledges protection to a free and independent medical profession.

To meet the needs of those unable to obtain proper medical attention, we recommend that a system of medical care be established by the proper state and local medical associations assisted when necessary by the state.

MEDICAL EXHIBITS AVAILABLE FOR LOAN

Exhibits pertaining to the work of the various departments of the American Medical Association or to subjects in which those departments are interested have been prepared and are available on a loan basis. The material falls into two groups:

Exhibits for medical societies and other scientific organizations.

Exhibits for the public for use at fairs and expositions.

Requests for material should be instituted as far in advance as possible, so that the proper reservations can be made. Requests from groups other than medical

societies should be made through the secretary of the local county or state medical society, or approval of such society obtained. Exact shipping addresses and dates should be given when the request is made.

Responsibility for installation and demonstration of the exhibits ordinarily must be borne by the organization to which the material is lent. The American Medical Association does not have the personnel for such duties.

Expenses include the items incidental to the installation and demonstration of the exhibit, as well as transportation charges.

A brief description of each exhibit is given in the following list. The notation is made whether the exhibit is intended for medical meetings or for public audiences; in a few instances both groups may be interested. The approximate amount of necessary wall space is indicated in linear feet; 30 linear feet could be provided in a straight line along the wall or around three sides of a booth 10 feet wide by 10 feet deep, with the side walls extended to the aisle in front. The electrical connections may be served either by alternating current or direct current unless otherwise noted; only 110 volts should be used, however. The shipping weights given are in approximate figures. Shipments will be made either by freight or by express, according to request.

Further information may be obtained from

Director, Scientific Exhibit
American Medical Association
535 North Dearborn Street
Chicago, Illinois.

1. What the Public Is Thinking About Health.

An exhibit from the Bureau of Health Education consisting of a mechanical display, summarizing 10,000 questions asked by the public; ten posters each 22 by 38 inches depicting various methods of disseminating health information; display files containing brief paragraphs on 200 health subjects.

Audience, public.

Space required, 25 linear feet of wall space (booth 10 by 10 feet with side walls extended out to front of booth.)

Electrical connections, one outlet, 150 watts, 110 volts, alternating or direct current.

Shipping weight, 380 pounds.

3. The Doctor Prevents Disease.

An exhibit from the Bureau of Health Education consisting of twelve posters, each 22 by 28 inches, showing means by which the physician may reach the public for the dissemination of health information.

Audience, medical.

Space required, about 14 linear feet of wall space.

Shipping weight, 44 pounds.

5. Information About Health.

An exhibit from the Bureau of Health Education consisting of two mechanical pieces about 45 inches high by 24 inches wide, with buttons for the visitor to push; six posters on health subjects, each 22 by 28 inches; three exposition files containing brief paragraphs on some 200 health topics; three exposition microscopes showing bacteria.

Audience, public.

Space required, about 16 linear feet of wall space, with a table in front 6 feet long (booth 10 by 10 feet with side walls).

Electrical connections, one outlet requiring about 200 watts.

Shipping weight, 477 pounds.

NOTE: One or both of the mechanical pieces can be eliminated, reducing the weight to 258 pounds.

6. The Human Factory.

An exhibit from the Bureau of Health Education consisting of three transparencies showing the human body in the form of a factory, the digestive system and the circulatory system; four posters, each 22 by 28 inches, depicting various functions of the "factory"; three models showing the skin, the head and the bladder; three display files containing brief paragraphs on topics in physiology.

Audience, public.

Electrical connections, six outlets, requiring about 600 watts, 110 volts, alternating or direct current.

Shipping weight, about 530 pounds.

8. Periodic Health Examinations.

An exhibit from the Bureau of Health Education consisting of one piece 8 feet long by 4 feet high containing transparencies

together with a transparent mirror with a button for visitors to push.

Audience, public.

Space required, 8 feet.

Shipping weight, 300 pounds.

9. Dangers of Self Diagnosis and Self Medication.

An exhibit from the Bureau of Health Education consisting of one piece 8 feet long by 4 feet high containing transparencies together with a transparent mirror with a button for the visitor to push; two mechanical pieces to be operated by the visitor; three exposition files containing information about home treatment, the home medicine cabinet and when to call the doctor.

Audience, public.

Space required, about 15 linear feet.

Electrical connections, about 900 watts.

Shipping weight, 543 pounds.

10. Nutrition.

An exhibit from the Bureau of Health Education consisting of two transparency cases, each about 45 inches high by 24 inches wide, showing various forms of malnutrition; nineteen posters in frames, each 24 by 30 inches, dealing with various aspects of nutrition; a large number of models of food products showing calories and other details, together with glass cases in which the models may be exhibited.

Audience, medical, public or other groups according to the demonstration.

Space required, about 30 linear feet of wall space.

Electrical connections, five outlets with a total of 500 watts.

Shipping weight, about 400 pounds.

11. Prevention of Accidents.

An exhibit from the Bureau of Health Education consisting of four panels, each 3 feet wide, equipped with legs and apron ready to set up, on which are posters dealing with traffic accidents, Fourth of July accidents, playground accidents and accidents in the home; mechanical "scrambler" carries appropriate messages; transparent mirror with buttons for the visitor to push showing appropriate cartoon; two exposition files containing brief paragraphs on some seventy-five items relating to accidents.

Audience, public and special groups.

Space required, 10 linear feet.

Electrical connections, two outlets, 300 watts, 110 volts, alternating or direct current.

Shipping weight, about 400 pounds.

12. Infant Welfare and Child Health.

An exhibit from the Bureau of Health Education consisting of eight posters, each 22 by 28 inches, dealing with various phases of antepartum care, infant feeding, and the like, and a mechanical piece with buttons for the visitor to push.

Audience, public.

Space required, 12 linear feet.

Shipping weight, about 100 pounds.

13. Medical Discoveries of a Century.

An exhibit from the Bureau of Health Education originally shown at A Century of Progress Exposition in Chicago, consisting of nine groups of figures—Beaumont, Morton, Pasteur, Lister, Roentgen, Theobald Smith, Curie, Ehrlich and Banting. Each group is set in a case with indirect lighting.

Audience, medical or public.

Space required, 16 linear feet (no back wall necessary).

Electrical connections, nine outlets, each for a 60 watt lamp.

Shipping weight, about 672 pounds.

14. Individual Health.

An exhibit from the Bureau of Health Education consisting of a series of twelve dioramas covering such subjects as nutrition, exercise and rest, weight control, correction of defects, avoidance of infection, and intelligence in health matters.

Audience, public.

Space required, 24 linear feet.

Electrical connections, twelve outlets, using a total of about 1,000 watts.

Shipping weight, about 951 pounds.

16. Your Health: The A. M. A. Broadcast.

An exhibit from the Bureau of Health Education dealing with the radio program of the American Medical Association consisting of a panel 4 feet wide by 6 feet high; an automatic bulletin board containing various messages; an automatic bar chart showing the number of responses to different types of programs; two exposition racks, one containing a Workbook for schools and the other for questions.

Audience, medical or public.

Space required, about 10 linear feet.

Electrical connections, two outlets requiring about 200 watts.

Shipping weight, about 352 pounds.

17. Information About Syphilis.

An exhibit from the Bureau of Health Education consisting of two transparency cases showing various syphilitic lesions; a large exposition microscope showing *Spirochaeta pallida*; an exposition file containing brief paragraphs on the subject of syphilis together with various charts and posters.

Audience, public.

Space required, about 15 linear feet.

Electrical connections, three outlets, about 600 watts.

Shipping weight, about 260 pounds.

18. Increase in Stature.

An exhibit from the Bureau of Health Education which was shown at A Century of Progress in Chicago, showing increase in stature from 1893 to 1933; one panel 3 feet wide by 6 feet high.

Audience, public.

Shipping weight, 157 pounds.

24. Prevention of Eye Injuries.

An exhibit from the Bureau of Health Education in conjunction with the Section on Ophthalmology of the American Medical Association, consisting of miscellaneous posters on panels ready to set up. The panels are accompanied by a transparency case showing transparencies of various eye injuries.

Audience, public.

Space required, 10 linear feet.

Electrical connections, three outlets, with a total of about 400 watts.

Shipping weight, 240 pounds.

25. Prevention of Burns.

An exhibit from the Bureau of Health Education, in conjunction with the Milwaukee Children's Hospital, consisting of miscellaneous posters on panels ready to set up and accompanied by a transparency case showing various injuries caused by burns. Where suitable arrangements can be made, a motion picture film on burns can be used with the exhibit. This will not be sent unless specifically requested. Motion picture, 16 mm., one reel, silent.

Audience, public.

Space required, 10 linear feet.

Electrical connections, two outlets with a total of about 400 watts.

Shipping weight, 240 pounds.

31. Information About Hospitals.

An exhibit from the Council on Medical Education and Hospitals consisting of a mechanical model of a hospital entrance with doors opening and shutting every four seconds to indicate how often a patient enters a hospital in the United States; shadow boxes and miscellaneous charts.

Audience, medical or public.

Space required, 15 linear feet of wall (or more according to selection of material).

Shipping weight, according to material selected.

32. Medical Education.

An exhibit from the Council on Medical Education and Hospitals consisting of charts showing statistics on medical education in the United States, together with miscellaneous maps and literature.

Audience, medical.

Space required and shipping weight, according to amount of material selected.

41. "Patent Medicines" and Quackery.

An exhibit from the Bureau of Investigation consisting of three mechanical pieces and twenty-eight posters, each 22 by 28 inches, with a literature rack for pamphlets.

Audience, public.

Space required, about 35 linear feet of wall for the entire exhibit, but selections can be made to accommodate a smaller area.

Shipping weight, about 350 pounds.

42. "Patent Medicine" Testimonials.

A small portion of exhibit 41 on "patent medicines" and quackery, which has been expanded, consisting of six posters, 22 by 28 inches, and two mechanical pieces.

Audience, public.

Space required, about 16 linear feet of wall.

Shipping weight, about 250 pounds.

46. Food Fads.

An exhibit from the Bureau of Investigation consisting of a mechanical piece; six posters each 22 by 38 inches and a "scrap-book," all dealing with some of the popular, but foolish, food fads.

Audience, public.

Space required, about 16 linear feet of wall.

Electrical connections, two outlets for 300 watts.

Shipping weight, 284 pounds.

47. Mechanical Nostrums.

An exhibit from the Bureau of Investigation showing a dozen fantastic mechanical contraptions for curing human ailments; display files containing brief paragraphs on many additional mechanical nostrums.

Audience, medical or public.

Space required, about 20 linear feet.

Shipping weight, 330 pounds.

51. Work of the Council on Pharmacy and Chemistry.

An exhibit from the Council on Pharmacy and Chemistry consisting of miscellaneous posters, each 22 by 28 inches, from which selections can be made to fit any space desired.

Audience, medical.

Shipping weight, from 40 to 50 pounds.

52. Work of the A. M. A. Chemical Laboratory.

An exhibit from the Chemical Laboratory, similar to the one from the Council on Pharmacy and Chemistry, consisting of posters from which selections can be made to fit any space desired.

Audience, medical.

Shipping weight, from 40 to 50 pounds.

53. Work of the Council on Foods.

An exhibit of the Council on Foods consisting of miscellaneous posters, each 22 by 28 inches, and an exposition "scrap-book" containing the various items of information concerning the work of the Council.

Audience, medical or public.

Space required, about 10 linear feet.

Shipping weight, according to amount of material selected.

54. Work of the Council on Physical Therapy.

An exhibit from the Council on Physical Therapy consisting of miscellaneous charts in frames, each 22 by 28 inches, together with selected apparatus. The following groups have been found

of interest: short wave diathermy; simple apparatus for physical therapy; miscellaneous posters dealing with the work of the Council.

Audience, medical.

Space required, variable according to kind of material selected.

Electrical connections, one or more outlets if mechanical material is selected.

Shipping weight, variable according to material selected.

55. Posture.

An exhibit from the Council on Physical Therapy consisting of four charts, each 22 by 28 inches, and six charts, each 36 by 26 inches.

Audience, public.

Space required, about 10 linear feet.

Shipping weight, 152 pounds.

56. Home Appliances for the Treatment of Poliomyelitis.

An exhibit from the Council on Physical Therapy consisting of charts in frames, each 22 by 28 inches; samples of home-made splints and a model of an underwater treatment tank, tools (vise, hammer, pliers), wire and padding material out of which the splints are made. Charts show the methods of making the splints, using the tools and material at hand.

Audience, medical.

Space required, booth about 10 feet wide by 7 feet deep.

Shipping weight, 100 pounds.

61. Medical Economics.

An exhibit from the Bureau of Medical Economics consisting of miscellaneous charts; a rack for literature showing the publications of the Bureau, two exposition files containing various items of information concerning medical economics, and an automatic bar chart showing physicians in various countries.

Audience, medical or public.

Space required, 30 linear feet or less, according to the kind of material selected.

Electrical connections, one outlet about 200 watts.

Shipping weight, 465 pounds.

66. Basic Science Laws.

An exhibit from the Bureau of Legal Medicine and Legislation consisting of six charts and frames, each 22 by 28 inches, together with a shadow box.

Audience, medical.

Space required, 15 linear feet.

Electrical connections, one outlet, 120 watts.

Shipping weight, 164 pounds.

67. Medical Legislation and Medicolegal Topics.

An exhibit from the Bureau of Legal Medicine and Legislation consisting of miscellaneous charts in frames, each 22 by 28 inches.

Audience, medical.

Space required, a booth of 15 linear feet.

Shipping weight, about 60 pounds.

71. Cutaneous Granulomas.

An exhibit from the Scientific Exhibit of the A. M. A., in conjunction with the Section on Dermatology and Syphilology, consisting of some 200 photographs and various granulomas. The photographs are mounted on eight panels, each 5 feet high and 3 feet wide with legs $2\frac{1}{2}$ feet high, which can be installed readily.

Audience, medical.

Space required, 24 foot back wall by 3 feet deep.

Shipping weight, 377 pounds.

72. Cutaneous Manifestations of Syphilis.

An exhibit from the Scientific Exhibit of the A. M. A., in conjunction with the Section on Dermatology and Syphilology, consisting of about 150 photographs of the various syphilitic lesions in different stages of the disease. The photographs

are mounted on panels 5 feet high by 3 feet wide with legs $2\frac{1}{2}$ feet high, which can be installed readily.

Audience, medical.

Space required, 18 foot back wall by 3 feet deep.

Shipping weight, 327 pounds.

73. Histopathology of Cutaneous Syphilis.

An exhibit from the Scientific Exhibit of the A. M. A., in conjunction with the Section on Dermatology and Syphilology, consisting of some seventy-five transparencies showing the histopathology of cutaneous syphilis.

Audience, medical.

Space required, 10 linear feet.

Electrical connections, three outlets requiring a total of 1,200 watts.

Shipping weight, 327 pounds.

77. Information About the American Medical Association.

An exhibit from the Scientific Exhibit of the A. M. A., consisting of two displays—one showing the history of the American Medical Association and the other showing the activities. Several literature racks are available to show the different publications, pamphlets and books which the Association publishes.

Audience, medical or public.

Space required, about 20 linear feet.

Electrical connections, two outlets with about 500 watts.

Shipping weight, 750 pounds.

78. Aesculapius, Hygeia and Hippocrates.

Three plaster plaques in bas-relief from the Bureau of Exhibits showing Aesculapius, Hygeia and Hippocrates. Each figure is $8\frac{1}{2}$ feet high, 3 feet wide, and 6 inches thick. Because of the fragile nature of the plaques, they will be sent only where they can be suitably installed.

Audience, medical or public.

Shipping weight, Aesculapius, 343 pounds; Hygeia, 354 pounds; Hippocrates, 300 pounds.

82. Treatment of Early Syphilis.

An exhibit from the Bureau of Exhibits, in conjunction with the United States Public Health Service, consisting of ten posters, each 22 by 28 inches, together with an exposition file containing various items of information about the treatment of early syphilis. (A duplicate of this exhibit can be obtained also from the United States Public Health Service, Washington, D. C.)

Audience, medical.

Space required, 15 linear feet.

Shipping weight, 125 pounds.

84. Treatment of Prenatal Syphilis.

An exhibit from the Bureau of Exhibits, in conjunction with the United States Public Health Service, consisting of ten posters, each 22 by 28 inches, together with an exposition file containing various items of information about the treatment of prenatal syphilis. (A duplicate of this exhibit can be obtained also from the United States Public Health Service, Washington, D. C.)

Audience, medical.

Space required, about 15 linear feet.

Shipping weight, 81 pounds.

86. Treatment of Late and Latent Syphilis.

An exhibit from the Bureau of Exhibits, in conjunction with the United States Public Health Service, consisting of ten posters, each 22 by 28 inches, together with an exposition file containing various items of information about the treatment of late and latent syphilis. (A duplicate of this exhibit can be obtained also from the United States Public Health Service, Washington, D. C.)

Audience, medical.

Space required, about 15 linear feet.

Shipping weight, 119 pounds.

91. *Hygeia* in Office, School and Home.

An exhibit from the Bureau of Exhibits, in conjunction with *Hygeia*, the Health Magazine, consisting of five dioramas showing the use of *Hygeia* in office, school and home.

Audience, public.

Space required, 10 linear feet.

Electrical connections, five outlets, requiring a total of 300 watts.

Shipping weight, about 250 pounds.

92. *Hygeia*, the Health Magazine.

An exhibit from the Bureau of Exhibits, in conjunction with *Hygeia*, the Health Magazine, consisting of two mechanical pieces; four exposition files with questions and answers from *Hygeia*, and miscellaneous posters.

Audience, public.

Space required, about 15 linear feet.

Electrical connections, two outlets, requiring about 200 watts.

Shipping weight, about 250 pounds.

94. *Hygeia* Display.

An exhibit from the Bureau of Exhibits, in conjunction with *Hygeia*, the Health Magazine, consisting of a mechanical model showing the various features of *Hygeia*, the Health Magazine (rising sun model).

Audience, public.

Space required, table 6 feet long by 2 feet wide.

Electrical connections, one outlet with about 200 watts.

Shipping weight, 148 pounds.

OFFICIAL NOTES

RADIO BROADCASTS

The fourth series of programs broadcast in dramatic form portraying fictitious but typical incidents of significance in relation to health by the American Medical Association and the National Broadcasting Company entitled "Your Health" began Wednesday, October 19, and will run consecutively for thirty-six weeks. The program is broadcast over the Blue network of the National Broadcasting Company each Wednesday at 2 p. m. eastern standard time (1 p. m. central standard time, 12 noon mountain time, 11 a. m. Pacific time).¹

1. Owing to program conflicts, there will be no Chicago broadcast of the network program. Instead, a recording of the program will be broadcast over Station WENR at 8 p. m. each Wednesday. This recording will be an identical rebroadcast of the network program broadcast earlier the same day.

These programs are broadcast on what is known in radio as a sustaining basis; that is, the time is furnished gratis by the radio network and local stations and no revenue is derived from the programs. Therefore, local stations may or may not take the program, at their discretion, except those stations which are owned and operated by the National Broadcasting Company.

The next three programs to be broadcast, together with their dates and their topics, are as follows:

November 2. Seeing and Hearing Well.

November 9. Healthier Boys and Girls.

November 16. Healthful Play.

Schools in the Chicago area that are planning to use the broadcasts as part of their health teaching program can tune in stations on the Blue network in nearby cities.

MEDICAL ECONOMIC ABSTRACTS

MATERNAL CARE IN MICHIGAN

The Division of Public Health Methods of the National Institute of Health of the United States Public Health Service has made a study of obstetric practices in Michigan. An elaborate questionnaire was sent to every attendant whose name was signed to any birth certificate in the state. The replies to this questionnaire form the base of the study, the results of which are summarized as follows:

The present study constitutes an attempt to determine the quality and distribution of maternal health services rendered to Michigan women during pregnancy and childbirth. The data consist, first, of approximately 21,000 birth certificates, which represent the number registered during the first quarter of 1936, and, second, of 10,000 detailed obstetric histories for a reasonably representative sample of these births. Study of the records results in the following observations regarding birth attendants and maternal services that were rendered:

Physicians attend 96.5 per cent of the registered births in the state, the remaining 3.5 per cent being about equally divided among doctors of osteopathy and a group of unspecified persons who are nurses, friends, relatives and neighbors of the pregnant women. Approximately one half of the physicians in the state are engaged in the practice of obstetrics, as evidenced by the fact that they delivered one or more babies during the first quarter of 1936. Physicians listed in the American Medical Directory as specialists and partial specialists in obstetrics or gynecology represent 9 per cent of the total group of birth attendants; this group delivers one sixth of the total number of births. Physician birth attendants in other medical specialties represent 17 per cent of the attendants and deliver another one sixth of the babies. Approximately 80 per cent of the births are attended by members of the American Medical Association, the remaining 20 per cent by nonmembers.

Study of the distribution of maternal services among the total group of attendants indicates that half of them—or less

than one fourth of the total number of physicians in the state—handle about 85 per cent of the births. The other half deliver the remaining one sixth of the babies. Maternal care given by obstetric specialists tends to be concentrated in the large cities; in rural areas this service is mostly in the hands of the general practitioners, especially those who graduated prior to 1915. A very small proportion of women living in rural districts have the services of obstetric specialists.

Antepartum care attaining the level of completeness that is advocated as an ideal standard is received by very few women. With respect to specific details of antepartum service, 13 per cent of the women have no urinalysis during this pregnancy, 16 per cent do not have their blood pressure recorded, 17 per cent have no abdominal examination, 32 per cent are not weighed, 21 per cent do not have the pelvis measured, and approximately two thirds are not known to have a serologic test for syphilis. Classification of antepartum care into broad groups with respect to its relative completeness and adequacy reveals that one fifth of the women receive what may be termed satisfactory care from a practical point of view, while one fifth receive wholly inadequate or essentially no professional antepartum service. Study of the distribution of this care shows a very marked correlation between the level of adequacy of antepartum service and economic status, the size of the city in which the mother lived and her parity. In general, women who are poor or who are on relief, women who live in rural areas and multiparous women bear the brunt of the widespread deficiency in antepartum services.

Nearly one half of the women studied are delivered in hospitals; those living in larger cities, those in the more comfortably situated classes and those having their first baby are more likely to have hospital care than women otherwise classified. Nearly 60 per cent of the mothers living in the larger cities, while less than 25 per cent of the rural women, are delivered in hospitals; according to economic status, hospitalization varies from 65 per cent among the comfortable, 59 per cent

among the moderate, 33 per cent among the poor to 28 per cent among those on relief. The proportion of primiparas hospitalized is nearly double that of multiparas.

Technics employed in the handling of labor and delivery were found to vary widely and to be related to certain characteristics of the birth attendant, to the place of delivery (home or hospital), to the size of the city and to the economic status of the family. If the procedures adopted by specialists in obstetrics are taken to represent standards of good practice, serious defects appear in the practices of many of the birth attendants. The most striking of these consist in the use of solution of posterior pituitary before delivery, in manual dilation of the cervix, in manual removal of the placenta, in the failure to use aseptic technic (sterile drapes and rubber gloves) and in frequent vaginal examinations and use of forceps. Taken as a group, the younger physicians, those who have graduated since 1925, tend to follow with slight variation the practices of the obstetric specialists; physicians who graduated before 1915, and in some instances the doctors of osteopathy, tend to adopt practices which are employed by the obstetricians with relative infrequency. Although questionable, and even dangerous, procedures are spread widely over the total group of parturient women, a relatively large share of the most serious defects in practice fall on poor women, those delivered at home and those living in rural communities.

Postpartum care, measured in terms of postpartum examinations, is given to less than three fourths of the women. The proportion of them receiving such care varies markedly with those factors which influence antepartum and parturient care.

These observations indicate broadly the deficiencies in maternal service as it exists at present in the state of Michigan. On the one hand, they indicate the complexity of the problem with its economic implications; on the other hand, they suggest some of the directions which attempts to improve material service must take.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ADDITIONAL MEDICAL COLLEGE NEWS APPEARS IN THE STUDENT SECTION, PAGE 1707.

ARIZONA

Refresher Courses.—Dr. John W. Amess, associate professor of pediatrics, University of Colorado School of Medicine, Denver, and Dr. Wilford W. Barber, Denver, are conducting lectures throughout the state under the auspices of the Arizona Board of Health in cooperation with the state medical association.

ARKANSAS

Personal.—The following have been appointed consultants to the state board of health: Drs. Alexander C. Kirby, pediatrics; Ernest H. White, obstetrics, and Herbert Fay H. Jones, syphilis control. All are of Little Rock.

District Meetings.—The Fifth District Medical Society was addressed in Camden October 6, among others, by Drs. Thomas D. Moore and Robert Lyle Motley, both of Memphis, on "Diagnosis and Treatment of Urinary Infections" and "Kidney Disease: Classification, Diagnosis and Treatment" respectively. Drs. William R. Brooksher and Sidney J. Wolfermann, Fort Smith, secretary and president respectively of the state medical society, also spoke. Dr. Wolfermann addressed the semi-annual meeting of the Second District Medical Society in Batesville October 10 on "What Constitutes a Good County Medical Society" and Dr. Alan G. Cazort, Little Rock, "Clinical Allergy As You See It."—The Sixth Councilor District Medical Society was addressed at DeQueen September 13 by Drs. George L. Carlisle, Dallas, on "Treatment of the Failing Heart"; George B. Fletcher, Hot Springs National Park, "Mental Depressive Psychoses"; Henry King Wade, Hot Springs National Park, "Urinary Infections"; Charles T. Chamberlain, Fort Smith, "Evaluation of the Systolic Murmur," and Ralph E. Weddington, Fort Smith, "Local Anesthesia in Obstetrics."

CALIFORNIA

University News.—Ground was broken at the University of Southern California, Los Angeles, recently for the new building for biologic research, the gift of G. Allan Hancock. The unit will be three stories high and will contain more than 100 laboratories for research in zoology, botany and related fields.

Graduate Conference in Gynecology.—The committee on graduate activities of the California Medical Association conducted a graduate conference on gynecology in San Diego October 17-20. Lecturers and their subjects included:

Dr. Daniel G. Morton, San Francisco, Menstrual Disorders and Cancer: Cervix and Uterine.
Dr. William B. Thompson, Los Angeles, Pelvic Infections from the Obstetric Aspect.
Dr. Erle Henriksen, Los Angeles, Pelvic Infections from the Gynecologic Aspect.
Dr. Donald G. Tollefson, Los Angeles, Benign Lesions and Uterine Tumors.

DISTRICT OF COLUMBIA

Personal.—Miss I. Malinde Havey, national director of public health nursing and home hygiene for the American Red Cross, died in Boston September 8. Miss Havey was decorated by the British and French governments during the World War for bravery under fire.

Society News.—Dr. Philip E. C. Manson-Bahr of the London School of Tropical Medicine addressed the Academy of Medicine of Washington September 28 on "The Life and Works of Patrick Manson, Father of Tropical Medicine." Dr. Harry H. Donnelly paid tribute to Dr. Earl B. McKinley, one of the founders of the academy, who recently was lost on the *Hawaii Clipper*.—At a meeting of the Medical Society of the District of Columbia October 12 a symposium on spotted fever was presented with the following speakers: Drs. Rolla E. Dyer, Ralph D. Lillie, Charles R. L. Halley, Harry A. Ong and Joseph F. Raffetto. Drs. Theodore J. Abernathy and Harry E. Dowling spoke October 19 on pneumonia, a résumé of recent prophylactic measures instituted in the District of Columbia.—Dr. Marvin Pierce Rucker, Richmond, Va., discussed "Toxemias of Pregnancy" before the Washington Gynecological Society October 22.

ILLINOIS

Society News.—The Adams County Medical Society was addressed in Quincy October 10 by Dr. Warren R. Rainey, St. Louis, on "Management of Acute Inflammatory Conditions About the Anus and Rectum."—Dr. Nathaniel G. Aleock, Iowa City, discussed malignancy of the kidney before the Rock Island County Medical Society, September 13, in Moline.—Dr. Lindon Seed, Chicago, discussed "Diseases and Infections About the Floor of the Mouth" before the St. Clair County Medical Society, Belleville, October 6.

Chicago

The Belfield Lecture.—Homer W. Smith, Sc.D., director of the physiologic laboratory, New York University, delivered the tenth annual William T. Belfield memorial lecture before the Chicago Urological Society October 27 on "Physiology of the Kidney."

Branch Meetings.—Dr. Archibald L. Hoyne will address the West Side Branch of the Chicago Medical Society November 18 on contagious diseases.—At a meeting of the Jackson Park Branch October 20 Dr. Robert B. Preble discussed "Trends in Medicine."—A symposium on diseases of the stomach and duodenum was presented before the Calumet Branch October 21 by Drs. Frederic T. Jung, Warren W. Furey, Rudolf Schindler, Fred M. Drennan and Warren H. Cole.—Dr. Cleveland J. White discussed "Diagnosis and Treatment of Demonstrated Skin Cases" before the Northwest Branch October 21.—The Irving Park Branch was addressed October 25 by Drs. Charles H. Parkes on "The Progress of Surgery During the Past Forty Years"; John R. Harger, "Evaluation of Present Surgical Procedures," and John H. Gilmore, "The Candid Camera in Medicine."—Dr. James G. Carr discussed angina pectoris before the South Chicago Branch October 18.—Dr. Arthur E. Hertzler, Halstead, Kan., addressed the Aux Plaines Branch October 28 on "Cardiovascular Effect of Nongonitrous and Toxic Thyroid."—Dr. Charles A. Doan, Columbus, and Edgar V. Allen, Rochester, Minn., will address the North Side Branch at the Drake Hotel at 8 o'clock November 3 on "Iron Metabolism and the Anemic States" and "Physiologic Effects of Extensive Sympathectomy for Essential Hypertension" respectively.

IOWA

Committee on Industrial Health.—The Iowa State Medical Society has appointed a committee on industrial health. Dr. Edward J. Harnagel, Des Moines, has been named chairman and Drs. Aldis A. Johnson, Council Bluffs, and William C. Goenne, Davenport, are members.

Society News.—Dr. William Malamud, professor of psychiatry, State University of Iowa College of Medicine, Iowa City, conducted a clinic in psychiatry before the Linn County Medical Society in Cedar Rapids October 21. Dr. Marius Nygaard Smith-Petersen, clinical professor of orthopedic surgery, Harvard University Medical School, Boston, discussed fractures of the hips. Dr. Benjamin L. Knight, Cedar Rapids, read a paper entitled "Review of Cancer Work."

Annual Fracture Clinic.—The second annual fracture clinic sponsored by the fracture committee of the Iowa State Medical Society was held in Des Moines October 20. The following participated:

Dr. W. Eugene Wolcott, Des Moines, Arthritis Associated with Fractures.
Dr. Dwight C. Wirtz, Des Moines, Fractures of the Hip, Blind Nailing.
Dr. Lewis M. Overton, Des Moines, Fractures of the Spine—Ambulatory Treatment.
Dr. Douglas N. Gibson, Des Moines, Patellar Injuries.
Dr. J. Albert Key, St. Louis, Emergency Treatment of Compound Fractures.
Dr. James E. M. Thomson, Lincoln, Neb., Fractures of the Forearm.
Dr. Walter D. Abbott, Des Moines, Emergency Treatment of Head Injuries.

MASSACHUSETTS

New England Graduate Assembly.—The first New England Postgraduate Assembly will be held at the Sanders Theater, Harvard University, Cambridge, November 15-16, with the following guest speakers:

Dr. Hubley R. Owen, Philadelphia: What Are the Duties and Responsibilities of the General Practitioner in the Treatment of Fractures? Unrecognized Fractures; Transportation of Injured and Emergency Treatment of Fractures with Special Reference to Fractures of the Long Bones and Fractures of the Spine; Skull Fractures and Concussion.
Dr. Alvah H. Gordon, Montreal: The Physician's Interest in Gall-bladder Disease; Mental Complications in Heart Disease; Diagnosis of Diseases with Coincident Enlargement of the Liver and the Spleen.
Dr. Harvey B. Stone, Baltimore: Preoperative and Postoperative Preparation of Surgical Patients; Symptoms and Signs of Intestinal Obstruction.
Dr. Perrin H. Long, Baltimore: Practical Interpretation of Laboratory Bacteriologic and Immunologic Diagnoses in Relation to Infectious Diseases; Clinical Use of Sulfanilamide in the Treatment of Bacterial Infections; Uses of Newer Derivatives of Sulfanilamide in the Treatment of Bacterial Infections.
Dr. Francis G. Blake, New Haven, Conn.: The Value of Antitoxin in Scarlet Fever; The Importance of Time in Serum Therapy.
Dr. Louis A. Buie, Rochester, Minn.: Office Methods of Diagnosis of Anal Diseases; Treatment of Common Anal Diseases.
Dr. Louis H. Nahum, New Haven, Conn.: The Etiology and Treatment of the Cardiac Arrhythmias.
Dr. Robert T. Frank, New York: Endocrinology as Now Practiced; The Female Sex Hormones.
Dr. William L. Estes Jr., Bethlehem, Pa.: Acute Traumatic Lesions of the Abdomen; Treatment of Open Wounds and the Use of Antiseptics.
Dr. Benjamin P. Watson, New York: When Is Cesarean Section Necessary and When Is It Unjustified? Treatment of Delayed Labor.

At the dinner Tuesday evening Dr. Warren F. Draper, executive officer of the U. S. Public Health Service, will discuss "Current Phases of the Problem of Medical Care" and Dr. Roger I. Lee, Boston, the private practice of medicine in the present social order. The assembly was authorized at the June meeting of the council of the Massachusetts Medical Society following the recommendation of its committee on graduate instruction. There will be a registration fee of \$3.

MICHIGAN

Annual Public Health Conference.—The eighteenth annual session of the Michigan Public Health Conference will be held at the Pantlind Hotel in Grand Rapids November 9-11. General sessions will be held in the Grand Rapids Civic Auditorium. The conference is sponsored jointly by the Michigan Department of Health and the Michigan Public Health Association. Organizations meeting in conjunction with the conference include the Michigan Association of Sanitarians, the State Organization for Public Health Nursing and the Michigan School Health Association.

Society News.—At the opening meeting of the Wayne County Medical Society, Detroit, for the 1938-1939 season, October 3, the speakers were Drs. Henry A. Luce, Detroit, and Thomas R. K. Gruber, Eloise, on the special session of the House of Delegates of the American Medical Association; Charles E. Dutches, Detroit, the Michigan State Medical

Society house of delegates; Louis J. Gariepy, Detroit, on Michigan public health legislation, and Sarah S. Schotten, the medical picture in Europe.—The second Northern Michigan Public Health Conference for the counties of Antrim, Charlevoix, Emmet and Otsego was held October 6; the speakers included Drs. Carleton Dean, Charlevoix; R. Philip Sheets, Traverse City; Loren W. Shaffer, Detroit, and Jerome T. Jerome, Traverse City.—Dr. Loren W. Avery, Chicago, discussed "Diagnostic Significance of the Hemiplegic and Paraplegic Syndrome" before the Calhoun County Medical Society in Battle Creek October 4.

MINNESOTA

New Health District.—Dr. Floyd M. Feldman, for two years head of rural health district 2 in Mankato, has been transferred to Rochester to organize a district health unit. The new unit will be the third established in Minnesota under the state department of health with federal social security funds. Dr. Feldman will be succeeded in Mankato by Dr. Frederick Gunnar Gunlaugson, Minneapolis, formerly epidemiologist of the state department of health. For the past year Dr. Gunlaugson has been studying at the Johns Hopkins University School of Hygiene and Public Health.

Meeting of Radiologists.—The Minnesota Radiological Society held its fall meeting in Rochester October 22. The following, all of Rochester, were among the speakers:

Dr. Charles K. Maytum, Use of X-Rays in the Treatment of Severe Asthma.
Drs. John D. Camp and J. Grafton Love, Intraspinal Protrusion of the Intervertebral Disks.
Dr. John L. Emmett, Value of Urography in the Differential Diagnosis of Obscure Abdominal Lesions.
Dr. John W. Olds, Treatment of Peyronie's Disease Using Radium.
Drs. Harry M. Weber and Charles Allen Good Jr., A Series of Interesting Duodenal Lesions.
Drs. Eugene T. Leddy and John A. L. McCullough, Treatment of Inoperable Carcinoma of the Breast by the Method of Multiple Converging Beams.

Dr. William C. MacCarty, Rochester, gave an address at the banquet on "Something About Specialism and Specialists."

MISSOURI

Health Forum.—Elmer V. McCollum, Ph.D., Baltimore, gave the first lecture in the fall series sponsored by the Jackson County Health Forum in Kansas City October 26; his subject was vitamins. Dr. Arthur T. McCormack, Louisville, also read a paper at this meeting entitled "Some Portions of Health Work." Dr. William W. Bauer, Director, Bureau of Health Education, American Medical Association, Chicago, will discuss "Popular Beliefs in Medicine That Are Not So" November 16 and Dr. Jay Arthur Myers, Minneapolis, December 21, tuberculosis. Dr. Morris Fishbein, Editor of THE JOURNAL, Chicago, will speak March 15. The forum was organized early this year under the auspices of the auxiliaries of the accredited hospitals of Jackson County and is approved by the county medical society.

NEW YORK

Outpatient Department Fifty Years Old.—The Rochester General Hospital, Rochester, celebrated the fiftieth anniversary of the opening of its outpatient department October 21. Dr. Albert C. Snell, for many years chief of staff at the hospital, recalled "Early Days in the O. P. D." and Mr. Ezra Hale, president of the board of directors, spoke on "Importance of the Clinic in the Community Health Program."

State Industrial Meeting.—The annual meeting of the New York State Society of Industrial Medicine will be held in Albany at the Ten Eyck Hotel November 3. The speakers will be:

Mr. William J. Picard, chairman, board of standards and appeals, state department of labor, The Dust Control Problem of the State Department of Labor.
Dr. Leroy U. Gardner, Saranac Lake, The Inhibitory Action of Other Minerals in Association with Silica.
Dr. Richard Kovacs, New York, Physical Therapy in Fracture Treatment.
Dr. Joseph Buchman, New York, A Résumé of the Post-Traumatic Osteoporoses.

Dr. Edgar A. Vander Veer, Albany, is president of the society.

New York City

First Harvey Lecture.—Guy F. Marrian, D.Sc., professor of biochemistry, University of Toronto Faculty of Medicine, Toronto, delivered the first Harvey Lecture of the season October 20 at the New York Academy of Medicine on "Some Aspects of the Intermediary Metabolism of the Steroid Hormones."

Friday Afternoon Lectures at the Academy.—The thirteenth series of Friday afternoon lectures at the New York Academy of Medicine will begin November 18 with a lecture by Dr. Harold T. Hyman on "Recent Advances in Therapeutics." Lectures for coming weeks will be:

December 2, Dr. Frank Fremont-Smith, Influence of Emotional Factors on Physiologic and Pathologic Processes.

December 9, Dr. Alan DeForest Smith, "Sciatic" Pain, Differential Diagnosis and Treatment.

December 16, Dr. Clarence E. de la Chapelle, Management of the Emergencies in Patients with Heart Disease.

Jan. 6, 1939, Dr. Howard Reid Craig, Diagnosis and Treatment of Some Diseases of the Newborn Infant.

Jan. 13, 1939, Dr. Walter C. Alvarez, Rochester, Minn., Functional Digestive Disturbances.

Therapeutic Use of Gases at World's Fair.—A division of pneumatology has been created by the New York World's Fair to direct the therapeutic use of gases as they are employed for the relief of pain (anesthesia), the saving of life (resuscitation) and clinical disease (oxygen therapy). The department will function in the double capacity of caring for visitors and as a practical demonstration of the most modern methods employed in this field, which may be studied by institutional and municipal groups. Suitable equipment will be provided to care for the following hazards: asphyxia from gases, drugs, submersion, fire fighting, foreign body obstruction, tumors within the airway, electrocution, strangulation, allergy, pressure due to moving objects, collapse of buildings, poisonous gases in manholes and premature asphyxia neonatorum. The Society for the Prevention of Asphyxial Death, Inc., is cooperating in the organization and development of this work.

OHIO

Annual Graduate Day in Toledo.—The Medical Institute of the University of Toledo presented its fifth annual Graduate Day October 28 at the university. The guest lecturers were Drs. John A. Toomey, Cleveland, on "Treatment of Meningeal Irritations," "Evaluation of Specific Vaccines and Serums in Prophylaxis and Treatment of Contagious Diseases" and "Management of Acute Contagious Diseases and Their Complications," and Louis E. Phaneuf, Boston, on "Significance of Menorrhagia and Metrorrhagia," "Pelvic Infection in Women" and "Management of Uterine Prolapse."

PENNSYLVANIA

State Medical Election.—Dr. Charles H. Hemminger, Pittsburgh, was named president-elect of the Medical Society of the State of Pennsylvania at the annual meeting in Scranton October 3-6. The following were elected vice presidents: Drs. Arthur E. Davis, Scranton; John B. F. Wyant, Kittanning; Walter J. Stein, Ardmore, and Arthur B. Fleming, Tamaqua. Dr. David W. Thomas, Lock Haven, became president. The 1939 session will be in Pittsburgh.

Society News.—Dr. Albert F. Doyle, Johnstown, assistant director, division of syphilis and genito-infectious diseases, state department of health, addressed the Butler County Medical Society September 13 on "The Duties of Physicians Treating Syphilis."—Dr. James L. Gilmore, Pittsburgh, addressed the Washington County Medical Society, Washington, September 14, on "Obstetrics for the General Practitioner."—At a meeting of the Westmoreland County Medical Society in Latrobe September 20 the speakers included Drs. Thomas St. Clair, Latrobe, and John F. Blair, Derry, on "Management of Bursitis" and "Management of Common Skin Conditions" respectively.—Dr. Robert C. Simpson, Ridgway, addressed the Elk County Medical Society July 12 on the mechanism of the electrocardiogram.

Philadelphia

Alvarenga Prize Competition.—The College of Physicians of Philadelphia announces that the Alvarenga Prize for 1939 will be awarded July 14, 1939, to the author of the best memorial or the best unpublished essay on any branch of medicine that may be deemed worthy. The committee will consider recent publications or unpublished typewritten manuscripts submitted to the committee before May 1. Manuscripts not in English must be accompanied by a translation in English. Address communications to the Alvarenga Prize Committee, 19 South Twenty-Second Street, Philadelphia.

Society News.—Among speakers before the Philadelphia Pediatric Society October 11 were Drs. Jacob B. Feldman on "Vitamin D Deficiency Related to the Eye" and Rutherford L. John, "Some Aspects of Osteochondritis Juvenilis."—Dr. Gerald H. J. Pearson, among others, addressed the Phila-

delphia Psychiatric Society October 14 on "The Chronically Aggressive Child."—A symposium on allergy will be presented during the winter before all the branch societies of the Philadelphia County Medical Society, as follows: Drs. Richard A. Kern, "General Principles of Allergy and Its Clinical Manifestations"; Louis Tuft, "Principles of Diagnosis and Treatment: Allergic Methods"; James Alexander Clark, "Bronchial Asthma," and Harry B. Wilmer, "Hay Fever and Other Allergies."—Drs. Bernard J. Alpers and Pascal F. Lucchesi addressed the Philadelphia County Medical Society October 19 on "Etiology and Pathology of Poliomyelitis" and "Treatment of Poliomyelitis" respectively.—Dr. Jesse G. M. Bullowa, New York, among others, addressed the Northern Medical Association of Philadelphia October 17 on "The Pneumonias."

VERMONT

State Medical Meeting and Election.—Dr. Edwin A. Hyatt, St. Albans, was elected president of the Vermont State Medical Society at its annual meeting in Burlington October 6. Dr. Angus C. Black, Brattleboro was elected vice president and Dr. Benjamin F. Cook, Rutland, secretary. The 1939 convention will also be held in Burlington. The guest speakers were:

Dr. Alexander D. Langmuir, Albany, N. Y., Serum Treatment of Pneumonia.

Dr. Wright Clarkson, Petersburg, Va., Carcinoma of the Cervix Uteri.

Dr. Philip J. Howard, Detroit, Convulsions in Infancy and Childhood.

Mr. R. F. Cahalane, director, Associated Hospital Service, Boston.

Group Hospitalization.

Friday morning October 7 a symposium on the gallbladder was presented by Drs. Alvan H. Gordon, Ralph R. Fitzgerald, Charles K. P. Henry and Joseph E. Pritchard, all of Montreal, Canada. In the afternoon a fracture demonstration was presented by the Vermont fracture committee of the American College of Surgeons, with Dr. Fred H. Albee, New York, as the guest speaker on "Destruction of the Blood Supply and Its Restoration in Fractures of the Hip."

VIRGINIA

Medical College Bequeathed One Million Dollars.—The Medical College of Virginia has received a bequest of securities valued at more than a million dollars from the estate of the late Mrs. Bettie Davis Wood. The gift will be added to the endowment funds of the college and used for general purposes. It will be known as the Judd B. Wood and Bettie Davis Wood Memorial, named for the late Dr. Wood, a Richmond dentist, and his wife.

State Medical Election.—Dr. Hugh H. Trout, Roanoke, was named president-elect of the Medical Society of Virginia at its annual meeting in Danville October 5. Drs. Perry W. Miles, Danville, and Samuel B. Moore, Alexandria, were elected vice presidents and Miss Agnes Edwards, Richmond, was reelected secretary-treasurer. Dr. Alex F. Robertson Jr., Staunton, was installed in the presidency, succeeding Dr. George F. Simpson, Purcellville. Richmond was chosen as the convention city in 1939.

WISCONSIN

Society News.—Dr. John D. Steele Jr. addressed the Milwaukee Academy of Medicine October 18 on "Management of Postoperative Pulmonary Complications with Special Reference to the Use of Intratracheal Suction." Dr. Samuel G. Higgins showed motion pictures of the work of medical missionaries in India.—Dr. Karl A. Memminger, Topeka, Kan., addressed the Medical Society of Milwaukee County, October 14, on "Psychiatric Problems in General Practice."

CANAL ZONE

Quarantine Against Yellow Fever.—The New York Times reported that a quarantine against yellow fever for passengers from Caribbean ports had been established in Balboa, October 3. The action was taken following the death in Guadalupe of the cook of a ship that had called at Venezuelan ports, although the point of infection had not been determined at the time of the report. The quarantine requires that passengers arriving by ship or plane have their temperatures taken daily for six days after leaving their last Caribbean port. Persons who have been vaccinated against yellow fever or who have recovered from it are exempted. This procedure supersedes the quarantine of ships' crews and passengers for six days for observation, it was stated.

GENERAL

Beware of Bogus Agent.—A hotel in Spencer, Iowa, has reported that a man giving the name A. J. Sutherland recently induced the hotel to cash a check for \$12.50 by claiming to sell publications of the American Medical Association. The man gave his address as 222 Fourth Street S.E., Cedar Rapids, Iowa, and claimed that he had just sold medical publications to the superintendent of a Spencer hospital. Accredited representatives of the American Medical Association are provided with credentials signed by Dr. Olin West, Secretary and General Manager.

Ike Luckman Wanted by Police.—The police department of the city of New York requests the cooperation of physicians in apprehending one Ike Luckman, charged with bribery and conspiracy. Luckman is 53 years of age and answers the following description: height, 5 feet 6 inches; weight, 200 pounds; brown eyes and hair; wears eye glasses, no rims; face slightly pockmarked; speaks Yiddish and English, and is neatly dressed. This man has diabetes and is believed to be a user of insulin. The police request that when located he be held as a fugitive from justice and the detective division of the department be advised by wire.

Railway Surgeons' Meeting.—The forty-ninth annual Congress of Railway Surgeons was held in Chicago at the Palmer House September 19-21. Among the speakers on the program were:

- Dr. John R. Nilsson, Omaha, Transportation and Treatment of Fractures.
- Dr. Roy W. Scott, Cleveland, Clinical Aspects of Cardiovascular Disease.
- Drs. Chevalier Jackson and Chevalier Lawrence Jackson, Philadelphia, Trauma of the Larynx.
- Dr. Dean D. Lewis, Baltimore, Nerve and Muscle Injuries.
- Dr. George F. O'Brien, Chicago, Pneumonia in Industry.
- Dr. Austin A. Hayden, Chicago, Conservation of Hearing.
- Dr. Vilray P. Blair, St. Louis, Acute Injuries of the Face.

Officers elected were Drs. Mathew A. Tinley, Council Bluffs, Iowa, president; Glenn I. Jones, Washington, D. C., Calvin A. Walker, San Francisco, and Leonard A. Ensminger, Indianapolis, vice presidents, and Daniel B. Moss, Chicago, secretary, reelected.

Fellowships for Cancer Research.—The Finney-Howell Research Foundation, Inc., announces that all applications for fellowships for next year must be filed in the office of the foundation, 1211 Cathedral Street, Baltimore, by January 1. Applications received after that date cannot be considered for 1939 awards, which will be made March 1, 1939. The foundation was provided for in the will of the late Dr. George Walker, Baltimore, for the support of "research work into the cause or causes and the treatment of cancer." The will directed that the surplus income from the assets of the foundation together with the principal sum should be expended within a period of ten years to support a number of fellowships in cancer research, each with an annual stipend of \$2,000 "in such universities, laboratories and other institutions, wherever situated, as may be approved by the board of directors." Ten fellowships were awarded in 1938.

Mortality Statistics for 1937.—The U. S. Bureau of the Census recently reported that the provisional crude death rate for 1937, as shown by death certificates received from state departments of health, was 11.2, as compared with the rate of 11.5 for 1936. The lowest rate ever recorded was 10.7 in 1933. There were 1,450,715 deaths, a decrease of 28,513 from the previous year. Thirty-three states and the District of Columbia showed decreases, six states showed no change and nine showed increases in rates. The highest rates were Arizona 16.8, New Mexico 15.2, District of Columbia 13.9 and Maine 13.4. The lowest rates were North Dakota 7.7, Oklahoma 8.4, South Dakota 8.6 and Arkansas 9. The bureau points out that differences in crude rates do not necessarily indicate corresponding differences in health conditions. Areas do not all have the same age, sex and racial distributions of the population and these factors, among others, partly determine the death rate.

WPA Publishes Index of Research Projects.—About 2,000 research projects carried on as part of the federal work relief program have been summarized briefly in an index and digest published by the Works Progress Administration, a volume of 291 pages. A concise statement of the conclusions of each study and an alphabetical index are included. Reports of these projects touch on nearly every field of natural and social science and many of them have appeared in scholarly journals in the form of articles. Many, however, are still in manuscript form and arrangements have been made with the American Documentation Institute whereby microfilm copies

of the original reports will be furnished at nominal rates to research specialists. A small edition of the index volume has been prepared for distribution to libraries, government departments, industrial concerns and research foundations. A limited supply is still available, the administration announces. Requests should be addressed to the Works Progress Administration, 1734 New York Avenue N.W., Washington, D. C.

Special Society Election and Council Actions.—The American Academy of Ophthalmology and Otolaryngology at its annual meeting in Washington, D. C., October 9-14, adopted a resolution expressing its "unqualified approval of those considerations relative to the national health program adopted by the House of Delegates of the American Medical Association in its special session held September 16-17." The academy also recommended to the appropriate governmental agencies that a nationwide vision and hearing survey of school children in the United States, incorporating necessary remedial measures, be undertaken. For such a survey the academy offered its technical and advisory services. Dr. Albert C. Snell, Rochester, N. Y., was chosen president-elect of the academy. Dr. George M. Coates, Philadelphia, will take office as president January 1. Vice presidents elected were Drs. William W. Pearson, Des Moines, Iowa; William J. Mellinger, Santa Barbara, Calif., and Charles A. Bahn, New Orleans. Dr. William P. Wherry, Omaha, was reelected executive secretary-treasurer and Dr. Secord H. Large, Cleveland, comptroller. The 1939 meeting will be in Chicago.

Changes in Status of Licensure.—The Massachusetts Department of Registration announces the following action:

Dr. David H. Shulman, Boston, license revoked August 18 because of gross professional misconduct in connection with the care of a premature termination of pregnancy.

The California State Board of Medical Examiners reports the following:

Dr. James H. Beggs, Idyllwild, Calif., license restored March 7.
Dr. Ralph A. Behrend, Keene, Calif., license restored March 8; placed on probation five years without narcotic privileges.

Dr. John V. Cocke, Los Angeles, license restored March 9; placed on probation five years without narcotic privileges and prohibition against indulgence in alcoholic or intoxicating liquors.

Dr. Arthur Lee Davis, Los Angeles, license restored March 9; placed on probation five years without narcotic privileges.

Dr. Thomas Flint Jr., San Francisco, license restored March 9; placed on probation five years without narcotic privileges.

Dr. George W. Fuller, formerly of Pasadena, Calif., license restored March 8; placed on probation five years.

Dr. Ernest D. Weaver, Los Angeles, license restored March 9; placed on probation five years without narcotic privileges.

Dr. Sharon M. Atkins, Los Angeles, license revoked March 9, for unprofessional conduct.

Dr. John Elmer Baker, Los Angeles, license revoked March 10, for conviction on an insurance fraud.

Dr. Paul F. A. Eid, Burlingame, license revoked March 10 for his conviction of a crime involving moral turpitude.

Dr. Oscar C. Long, Brawley, Calif., license revoked March 10 for federal narcotic conviction.

Dr. Frank Adrian Pearl, Los Angeles, license revoked March 10, for his conviction of an insurance fraud.

The Delaware state board reports:

Dr. Frank R. Palmer, Wilmington, license revoked June 22 for performing an illegal operation which resulted fatally.

The Michigan State Board of Registration announces the following action:

Dr. Leo Charles Donnelly, Detroit, license revoked June 16 for unprofessional advertising.

The Minnesota State Board of Medical Examiners reports the following:

Dr. Nels G. Mortensen, St. Paul, license revoked July 16 for two years; he was found guilty of "immoral, dishonorable and unprofessional conduct" and specifically with "procuring, aiding and abetting a criminal abortion."

FOREIGN

Congress of Comparative Pathology.—The fourth International Congress of Comparative Pathology, to be held in Rome May 15-20, 1939, will have three sections, it was recently announced. They will be human medicine, veterinary medicine and phytopathology. Papers submitted to any section must be related to the main topic and be as concise as possible. A summary of about 100 words should also accompany the papers, which must be submitted by March 31, 1939. Among those listed to take part in the discussions are Wendell M. Stanley, Ph.D., Princeton, N. J.; Sir Aldo Castellani, Rome, and Prof. G. Ramon, Paris.

Deaths in Other Countries

Dr. Karl Sudhoff, for years professor of the history of medicine at the University of Leipzig, died in Salzwedel, Germany, October 14, aged 84.

and head of the department of urology in the Faculté de médecine (medical school of the University of Paris). Professor Chevassu's clinic at the Cochin Hospital has been visited by many American urologists, and his many contributions to the literature of urology have made his work familiar to urologists all over the world.

A Curie Postage Stamp

A new postage stamp, of a denomination corresponding to the 5 cent American stamp, has been issued in honor of the discoverers of radium, Professor and Madame Curie. It is being sold with a slight additional tax, which is destined to aid the work of the International Union against Cancer, whose meeting will be held shortly in connection with the anticancer week.

BERLIN

(From Our Regular Correspondent)

Sept. 17, 1938.

The Decline of Consanguineous Marriages

Prof. Dr. Fritz Lenz, Berlin ordinarius, recently published in *Erbarzt* a report on the incidence of consanguineous marriages. Medical geneticists regard such marriages as dangerous because of the frequent exaggeration of the transmitted recessive pathologic characters. Moreover, such marriages are of importance to research on defective heredity. The problem is approached in the following manner: The records of a large number of cases of a particular disorder, deaf-mutism for example, are assembled, and determination is made of the percentage of consanguineous marriages which have taken place in the ascendencies. To make sure that this percentage is greater than the incidence of consanguineous marriages in the population as a whole, one must be conversant with the latter figure. But the incidence in the population will differ at various times, in various localities and in various groups. Acceptable, useful statistics are available from Prussia, where, since 1875, the marriage

Consanguineous Marriages in Prussia

Decade	Percentage
1875-1884	0.78
1885-1894	0.62
1895-1904	0.48
1905-1914	0.43
1915-1924	0.30
1925-1934	0.17

registries have kept routine records of all marriages contracted between first cousins, uncles and nieces, and aunts and nephews. The percentages of such marriages to the total number registered in the various decades are shown in the accompanying table.

In the years 1934, 1935 and 1936 the corresponding percentage remained 0.11. Accordingly, in six decades the incidence of marriages between blood relations has greatly decreased. As the principal cause of this trend, Lenz cites the migrations of the population within the reich as well as the greater concentrations of people in large cities and industrial centers. In the urban community kinfolk tend to drift apart or lose track of one another much more readily than in the country. Another important factor is decreased natality. During the seventies the average number of births per marriage was five; in the last decade it was only two. At the rate of five births per marriage every male citizen would have on an average twenty female first cousins, one of whom he might eventually marry; but if an average of only two children result from a marriage, the corresponding figure is two instead of twenty. The probability of marriage among blood relations has therefore decreased in the course of six decades much more rapidly than the birth rate. On the other hand, the incidence of marriages between more distant relations will not decrease as rapidly as the incidence of marriages between the nearer of kin. The common ancestors of second and even more distant cousins belong one or more

generations further back in the ascendancy. Accordingly, the decline in the birth rate, which first became substantial around the turn of the century, can have exerted scarcely any influence on the incidence of marriages between more distant relatives, although it has already influenced to a certain extent the incidence of the more consanguineous unions. Marriages of first cousins outnumber the marriages of other near relatives by about 10:1.

If one wishes to evaluate the percentage of such marriages in the parentage of a particular group of sick persons, one must compare the figures with the average percentage for the decade during which the parents in question were married (by reference to the figures quoted by Lenz). Knowledge of these statistics is likewise valuable for the prognosis of the incidence of recessive hereditary disorders. As about one third of all deaf-mutes are children of consanguineous marriages, a recession in the incidence of such unions would be accompanied by a substantial decline in the incidence of deaf-mutism. The decreased incidence of this condition is of course based also on a decrease in the morbidity of meningitis, scarlatina and syphilis. Lenz states further that the majority of recessive hereditary disorders are found not in the progeny of close blood relations but in that of more distant relatives, even in the offspring of parents who are themselves unaware of any kinship yet come from the same community or from the same rural group. Since marriages of more distant relatives tend to decrease in frequency much less rapidly than marriages of near relatives, the decline in the incidence of congenital defects transmitted by the former will progress at a slower pace than those transmitted by the latter. At all events, the decreasing incidence of consanguineous marriages should be considered an important factor in the decline of recessive hereditary disorders.

More About the Exclusion of Jewish Physicians

To the new decree by which the licenses of all Jewish physicians are revoked, several additional rules and stipulations have been appended. As already reported, a certain number of Jews will still be issued special permits to practice in the Jewish community, but only in the biggest cities, such as Berlin and Vienna, which contain a large Jewish population. In Berlin, for example, 200 Jewish physicians will be allowed to remain in practice after September 30, in order, as officially stated, to prevent a rush of Jewish patients to the Aryan practitioners. The special permits issued to Jewish physicians will by no means approximate the regular license (approbation) but will be in the nature of temporary authorization to practice medicine. These Jewish practitioners will even be officially designated not as "physicians" (*aerzte*) but as "treaters of the sick" (*krankenbehandler*). The latter is a term recently used by Privy Councillor Dr. Conti, director of the central municipal health bureau of Berlin and a powerful Nazi influence in medical affairs. The residences of Jewish doctors who remain in practice must be identifiable by special legends. It is stipulated that in cities (except Berlin and Vienna) which contain Jewish hospitals no Jew may engage in outside practice. Among places in which this rule will be enforced are Hamburg, Cologne, Frankfurt on the Main and Breslau, although all these cities have large Jewish populations. Whether this regulation will remain long in force cannot at present be stated. Permits to practice certain specialties not represented in the Jewish hospitals may be issued to Jewish physicians in the localities affected.

In future Jewish patients may be admitted only to Jewish clinics and hospitals or to those institutions which, as Dr. Conti phrases it, "because of their sectarian character remain in down-right ignorance of racial and national questions." This last reference is to certain non-Jewish sectarian hospitals and other hospitals under private charitable direction. Despite numerous declarations to the contrary, the expulsion of Jewish physicians, as already reported, bids fair to produce an acute shortage of

practitioners. This is evidenced by a notice that appeared late in August in the Berlin *Abendblatt*, a Nazi party organ, to the effect that a temporary lack existed in the medical service available to Berliners, especially in six areas in the northern, eastern and southern sections of the city inhabited by the lower income groups of the population. A landlord can now on short notice break a lease with a Jewish physician who is being forced out of practice. The same issue of the newspaper also carried a stern and emphatic warning to all landlords in question against failure to take advantage of this opportunity to get rid of their Jewish tenants within a reasonable time and to reserve the vacated premises for new non-Jewish practitioners.

AUSTRALIA

(From Our Regular Correspondent)

Sept. 1, 1938.

Examination of Men Exposed to Lead

Criticisms of the estimation of the ratio of large to small lymphocytes as a practical laboratory method in the examination of men exposed to lead and of the common method of estimating the strength of the hand grip were advanced recently by Dr. L. A. Windsor-McLean, chairman of the medical (lead poisoning) board, Mount Isa Mines, Queensland. The criticism concerning the former method was that if a division of the lymphocytes is made merely on a consideration of absolute size (e. g. 10 micromillimeters) too many uncontrollable factors are involved for the estimation to be of general use. The spreading of the blood film makes a vast difference in the apparent size of all the blood cells, and even on one film the ratio of large to small lymphocytes was found to vary as much as from 9 in a thin portion of the smear to 1.1 in a thick portion. Also, contrary to the opinion that the strength of the hand grip is the most generally useful test in the search for lead poisoning, it is felt by Dr. Windsor-McLean that the test is thoroughly unreliable, at least as far as estimating the strength of the hand grip. by using a Collins type dynamometer is concerned. He considers that there is no guaranty that the subject is using the maximum effort of which he is capable and cites the case of a man applying for compensation. Apart from this subjective aspect of the readings, he considers that in many cases the maximum reading is determined by the pain produced by the instrument rather than by muscular strength. Finally, a definite knack may be acquired whereby, as a result of a sudden squeeze, a momentarily high reading may be obtained.

DARK FIELD EXAMINATION FOR POLYCHROMASIA

In view of Lane's dictum that after exposure to lead and before the appearance of stippled cells in the blood a high polychrome count is frequently the only change found, an original method of examination for polychromasia with dark field illumination has been described. Ordinary thin blood films are made, dried and fixed and then treated with Sellers's stain. In a microscopic examination with a "cardiod" dark ground condenser, the ordinary orthochromatic cells show up as yellow rings, while the polychromatic cells are pink to reddish pink rings. The fact that these pink cells actually correspond to the polychromatic cells has been amply verified. It is contended that with practice one can pick out the polychromatic cells, like the stippled cells, more readily in the dark field and that a dark field is certainly much easier on the eyes of any one who must do large numbers of counts during a day.

Research in New Zealand

Under the provision of the health act, the New Zealand government has established a medical research council, all the members of which are physicians with the exception of the director general of scientific and industrial research. A statutory function of the health department is to promote or carry out

researches and investigations in matters concerning the public health and the prevention or treatment of disease. This council will act solely in an advisory capacity to the minister of health and will not control expenditure. Committees will be appointed as part of the organization to supervise each investigation, and adequate funds will be provided by the government. Preliminary research work has already been done under the auspices of the department of health. Subjects for present and future investigation include nutrition, tuberculosis, goiter, dental caries, hydatid disease, cancer and undulant fever. Since 1924 the government has provided only £13,239 for medical research in New Zealand, and payments have been intermittent. This recent move gives promise of medical research on a more definite and liberal plan, coordinated with similar work being done in England and Australia.

Consumption of Dangerous Drugs

On a per capita basis, the consumption of heroin, morphine and cocaine in Australia is much higher than the world average. The League of Nations report for 1936 showed that Australia consumed 7.5 per cent of the heroin and 14 per cent of the morphine accounted for. The accompanying table indicates the consumption in kilograms per million of inhabitants for the years 1931 and 1934. The figures show that morphine and heroin are used four times as extensively in Australia as in Great Britain and that, although the American figure for morphine is higher than the Australian, this country uses almost 400 times the amount of heroin consumed in America. The use of cocaine is twice as great in Australia as in America or Great Britain. These figures suggest that the taking of potent

Consumption of Dangerous Drugs

	1931	1934
Morphine		
Great Britain	17.72	3.90
United States	16.89	17.19
Australia	12.97	13.36
New Zealand	9.96	9.70
Heroin		
Great Britain	1.09	0.98
United States	0.06	0.01
Australia	3.10	3.90
New Zealand	1.99	0.65
Cocaine		
Great Britain	5.48	5.00
United States	6.88	6.37
Australia	12.97	12.76
New Zealand	5.31	4.52

drugs is greater here than is generally imagined. Legislation to amend the regulations relating to dangerous drugs and poisons, with a view to more effective control over the consumption of these materials, is at present under consideration in several of the Australian states.

Dr. W. B. Castle Lectures in Australia

Primarily at the invitation of the permanent postgraduate committee of the Victorian branch of the British Medical Association, Dr. W. B. Castle, director of Thorndyke Memorial Laboratories and of the City Hospital, Boston, delivered six postgraduate lectures. Subsequently, by arrangement with the state postgraduate committees, he gave further lectures and demonstrations in Sydney and Brisbane. Dr. Castle took as his subjects the pathologic physiology and classification of the anemias, the etiology of nutritional deficiency anemias, the diagnosis and treatment of anemias, the hemorrhagic diseases, the general consideration of vitamin deficiencies and the clinical manifestations of vitamin deficiencies. He referred to anemia as a physiologic rather than a morphologic problem. The importance of anoxemia as a marrow stimulant was stressed. The function of the spleen is a mystery. Stippling of the red cells is a form of reticulocytosis. The greatly increased need

for iron in women was emphasized. Chlorosis has not disappeared. Administration of iron is essential in the treatment of hookworm disease. Condemnation of many of the commercial iron and liver preparations on the market was expressed, and the new "efficiency unit" of liver preparations was announced. In the lectures on the hemorrhagic diseases, the effect of the recently discovered vitamin K was described. Although splenectomy in the treatment of thrombopenia increases the platelets in the circulating blood, it is not otherwise a specific measure. The platelets are antigenically related to the vascular endothelium. Hodgkin's disease is a megakaryocyte tumor. The fundamental defect in hemophilia is the slow conversion of prothrombin into thrombin. In this disease also the platelets are not backed up by proper fibrin formation.

The visit of Dr. Castle was valuable not only for the refreshingly modern understanding of blood pathology that he conveyed but also for the impetus he gave to graduate education and study. He also played an important part in cementing the medical associations of America and Australia. In his concluding remarks he extended an invitation to Australian medical graduates to visit the United States and offered to facilitate their wishes regarding the institutions or centers they might wish to visit. He styled himself a future unofficial Australian ambassador in America. It is hoped that Dr. Castle's tour is but a prelude to further visits of American medical scientists of similar high caliber.

POLAND

(From Our Special Correspondent)

Sept. 24, 1938.

The Prevention of Lead Poisoning in Foundries

In the State Institute of Hygiene at Katowice, Polish Silesia, Dr. Jan Adamski has performed systematic examinations of blood smears from 3,000 workers in lead and zinc foundries. He studied the percentage of basophilic red cells, estimating the number at 200 per million cells as evidence of lead poisoning. The results have shown that the percentage of poisoned workers is approximately the same in the zinc foundries as in the lead foundries, although zinc ore contains much less lead than lead ore. The relatively high incidence of lead poisoning in the zinc industry is probably due to the inadequacy of health protection in zinc foundries in comparison with that in the lead industry. The author found that mass blood examinations for basophilic spotting of red cells is the method of choice for discovering lead poisoning, especially in the earliest stages of the disease. He requires blood examinations to be repeated regularly every three months on all factory workers who are exposed to lead.

Typhoid in Warsaw

As a large increase in typhoid has been observed in Warsaw every autumn, the boards of health have taken prophylactic measures. The number of wards for typhoid in the hospitals has been enlarged; the hygienic state of food supplies, especially in fruit shops and dairies, has been controlled by the health authorities, and the population has been instructed by popular lectures and posters about means of prevention.

"Epidemic Physicians"

The Ministry of Labor and Social Welfare has created lists of "epidemic physicians." These physicians are sent to places where an increase in epidemic diseases has been observed, in order to organize prophylaxis and therapy.

Exhibition of Hospital Organization

The first exhibition of the Polish hospital organization was opened in Warsaw in September. The part played by the hospitals in public health and their activity in controlling infectious diseases were demonstrated. The section of architecture for hospitals presented the general ideas in the building of hospitals

and in their interior fittings. The interiors of all the hospitals in Poland were illustrated. The exhibition was much frequented by the public, who listened to talks on hygiene with great interest.

The Reduction in Prices of Drugs

To make reasonable the prices of medicines for the poor, the authorities ordered the pharmacists to cut the prices of all drugs by 10 per cent. In addition there was prepared a list of about 100 drugs which have to be supplied to the unemployed at cost price.

Marriages

GRADY CORNELL SISKE, Pleasant Garden, N. C., to Miss Robbie Emily Dunn of Greensboro in High Point, August 22.

MELVIN SCHURAK, Hot Springs National Park, Ark., to Miss Elaine Kessler of White Castle, La., in August.

ROBERT GORDON JOHNSTON, New Haven, Conn., to Miss Eleanor Talcott Fisher of Orinda, Calif., August 12.

HUGH CABOT, Rochester, Minn., to Mrs. Elizabeth Cole Amory of Boston, in Hingham, Mass., October 8.

JOHN McIVER JACKSON, Front Royal, Va., to Miss Rachel Jackson Blythe at Huntersville, N. C., in June.

WALTER HENRY JAESCHKE to Miss Inga Walfus, both of Madison, Wis., in Rockford, Ill., in September.

JAMES ROBERT SHANKLIN, Bluefield, W. Va., to Miss Helen Throck Morton of Arlington, Va., August 10.

RALPH FOSDICK SPENCER, Hudson, N. Y., to Miss Mary Elizabeth Puleston of Sanford, Fla., August 5.

JAMES FLOURNOY MARSHALL to Miss Mildred Gordon Coleman, both of Winston-Salem, N. C., June 4.

FRANKLIN I. HARRIS to Miss Alleene Dunker, both of San Francisco, at Carson City, Nev., August 16.

DAVID OSCAR SMITH, Washington, D. C., to Miss Grace Henderson of Monroe, N. C., September 3.

EDWARD JOHN PURCHLA, Chicago, to Dr. Rose Hedwig KWAPICH of Toledo, Ohio, September 27.

HERMAN L. MELTZER, Clinton, Ill., to Miss Elsie Thornton of Farmer City in St. Louis, August 18.

CHARLES W. MATTHEWS to Miss Thelma Juanita Carey, both of New Vienna, Ohio, in August.

TOM HALL MITCHELL to Miss Mazie F. Moore, both of Mobile, Ala., in Tulsa, Okla., July 29.

WALTER SIMMONS JR., Charleston, S. C., to Miss Ruth Wackerman of Norfolk, Va., in June.

THEODORE WINSLOW JONES to Miss Elizabeth Gamwell, both of Pittsfield, Mass., September 30.

RAYMOND JOHNSON SHERER, Jasper, Ala., to Miss Barbara Farrar Palmer of Dora recently.

DONALD C. SHARPE, Verona, Wis., to Miss Lorraine Nauman of Dubuque, Iowa, June 25.

JOHN HOBART JUDSON, Arlington, Va., to Miss Joyce Mary Duffield of Miami, Fla., in July.

VERNE CLIFTON LANIER, Welcome, N. C., to Miss Lela Hedrick of Lexington, June 30.

WILLIAM EDWARD BRETZ to Miss Ruth Emily Converse, both of Hinsdale, Ill., September 10.

CLARE C. JONES to Miss Doris Kintz, both of Spencer, Iowa, in Sioux Falls, S. D., July 25.

SIDNEY A. SLATER, Worthington, Minn., to Mrs. Charles Moulton Smallwood, June 17.

OWEN DANIEL MOORE, Knoxville, Tenn., to Miss Emily Roberts of Etowah, July 26.

HAROLD LAWTON ROGERS, Albertville, Ala., to Miss Frances Love McKenzie in July.

CECIL E. JOHNSON, Rensselaer, Ind., to Miss Gladys Culp of Francesville, July 28.

EDGAR W. MEISER to DR. MARY ELLEN SMITH, both of Lancaster, Pa., July 23.

JOHN J. SAZANA JR., Brookfield, Ill., to Miss Sonia Gorecki of Chicago, August 20.

PAUL R. MIRAGLIA, Conshohocken, Pa., to Miss Eleanor De Marino, June 4.

Deaths

Andrew Johnson Crowell, Charlotte, N. C.; University of Maryland School of Medicine, Baltimore, 1893; member of the House of Delegates of the American Medical Association, 1909, 1915, 1922, 1925, 1926, 1929, 1930 and 1931; member of the Medical Society of the State of North Carolina; past president of the Mecklenburg County Medical Society and the Tri-State (Carolinas and Virginia) Medical Society; member of the American Association of Genito-Urinary Surgeons and the American Urological Association; fellow of the American College of Surgeons; past president of the North Carolina Urological Association; past president of the state board of health; on the staffs of the New Charlotte Sanatorium and the Presbyterian Hospital; at one time secretary and treasurer of the North Carolina Medical College and professor of genito-urinary surgery; aged 71; died, September 21, in a local hospital of carcinoma of the stomach.

Franz John A. Torek * New York; College of Physicians and Surgeons, Medical Department of Columbia College, New York, 1887; member of the American Surgical Association; fellow of the American College of Surgeons; past president of the American Association for Thoracic Surgery; adjunct professor of surgery at the New York Post-Graduate Medical School and Hospital 1899-1915; consulting surgeon and formerly attending surgeon to the Lenox Hill Hospital; for many years attending surgeon to the New York Skin and Cancer Hospital; originator of the Torek operation for undescended testicle; contributor of a chapter on thoracic surgery in Johnson's "Operative Therapeutics" and on esophagectomy in "Cyclopedia of Medicine"; aged 76; died, September 19, in Vienna of bronchopneumonia.

Winfield Scott Farmer * Nashville, Tenn.; Vanderbilt University School of Medicine, Nashville, 1890; member of the American Psychiatric Association; instructor in clinical psychiatry at his alma mater; medical superintendent of the Central State Hospital; aged 71; died, August 5, in the Vanderbilt Hospital of bronchopneumonia and carcinoma.

John Francis McCusker, Providence, R. I.; College of Physicians and Surgeons, Medical Department of Columbia College, New York, 1889; fellow of the American College of Surgeons; formerly connected with the U. S. Public Health Service; aged 72; died, August 27, in the Rhode Island Hospital of cerebral hemorrhage.

Edward Taylor Hull, New York; Columbia University College of Physicians and Surgeons, New York, 1904; fellow of the American College of Surgeons; on the staff of the Lincoln Hospital; aged 58; died, August 29, in the Lenox Hill Hospital of hemorrhage into the thalamus due to hypertensive cardiovascular disease.

Carroll D. Evans, Columbus, Neb.; College of Physicians and Surgeons, Baltimore, 1882; member of the Nebraska State Medical Association; fellow of the American College of Surgeons; on the staffs of the Columbus and St. Mary's hospitals; aged 82; died, August 12, of gangrene, sepsis and arteriosclerosis.

Joseph Aspray, Spokane, Wash.; Tufts College Medical School, Boston, 1902; member of the American Roentgen Ray Society and the Radiological Society of North America; served during the World War; aged 59; died, August 20, in the Sacred Heart Hospital of uremia, arteriosclerosis and hypertension.

Robert Wayne Nosker * Columbus, Ohio; Ohio State University College of Medicine, Columbus, 1917; served during the World War; aged 44; on the staffs of the Grant Hospital, St. Francis Hospital, Children's Hospital and the White Cross Hospital, where he died, August 26, of rheumatic heart disease.

Isaac Eldridge Huff, Roanoke, Va.; College of Physicians and Surgeons, Baltimore, 1892; member of the Medical Society of Virginia; past president of the Roanoke Academy of Medicine; on the staff of the Shenandoah Hospital; aged 72; died, August 17, of coronary thrombosis and pneumonia.

Czar Clinton Johnson * Lincoln, Neb.; John A. Creighton Medical College, Omaha, 1907; lecturer on industrial hygiene at his alma mater; fellow of the American College of Surgeons; served during the World War; on the staff of St. Elizabeth's Hospital; aged 57; died, August 21, of coronary thrombosis.

John Thomas McDonald, Brawley, Calif.; University of Louisville (Ky.) Medical Department, 1900; served during the World War; at one time connected with the U. S. Veterans Bureau and Veterans Administration; aged 64; died, July 31, in Los Angeles of arteriosclerosis.

Clyde Achillis Eckler, Dry Ridge, Ky.; Miami Medical College, Cincinnati, 1902; member of the Kentucky State Medical Association; past president and secretary of the Grant County Medical Society; aged 61; died, August 10, of hypertensive cardiovascular disease.

William Wallace Cornog, Lavonia, Ga.; Atlanta Medical College, 1888; formerly mayor and chairman of the school board; served during the World War; aged 73; died, August 25, in the Veterans Administration Facility, Atlanta, of myocarditis and arteriosclerosis.

George Nelson Heilig, McClure, Ill.; Barnes Medical College, St. Louis, 1902; member of the Illinois State Medical Society; member of the board of education; aged 61; died, August 16, in the Southeast Missouri Hospital, Cape Girardeau, Mo., of angina pectoris.

James Morgan Ballew, Memphis, Texas; Louisville (Ky.) Medical College, 1891; member of the State Medical Association of Texas; served during the World War; aged 75; died, August 12, in a sanatorium at Excelsior Springs, Mo., of congestive heart disease.

Frank H. Hancock, Norfolk, Va.; University College of Medicine, Richmond, 1896; member of the Medical Society of Virginia; served during the World War; formerly county health commissioner; city physician; aged 65; died, August 15, of cirrhosis of the liver.

George Preston Wintermute, Berkeley, Calif.; Jefferson Medical College of Philadelphia, 1893; formerly clinical instructor in surgery (otology, rhinology and laryngology) Stanford University School of Medicine; aged 67; died, July 15, of coronary occlusion.

Martin Lewis Tirrell, New York; University of the City of New York Medical Department, 1893; member of the Medical Society of the State of New York; aged 74; died, July 31, in St. Luke's Hospital of pyelonephritis, chronic cystitis and bronchopneumonia.

Victor Leo Arthur Langenderfer * Toledo, Ohio; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1909; aged 51; formerly on the staff of St. Vincent's Hospital, where he died, August 7, following an operation for appendicitis.

Monsell Ray Bell, Keyser, W. Va.; University of Maryland School of Medicine, Baltimore, 1903; member of the West Virginia State Medical Association; aged 59; died, August 31, in the Allegany Hospital, Cumberland, Md., of myocarditis.

Walter E. Mitchell * Bushnell, Fla.; Southern College of Medicine and Surgery, Atlanta, Ga., 1914; secretary of the Sumter County Medical Society; aged 54; died, August 24, in a hospital at Atlanta of cerebral hemorrhage, arteriosclerosis and nephritis.

Francis B. Fite, Muskogee, Okla.; Southern Medical College, Atlanta, 1886; fellow of the American College of Surgeons; at one time mayor; on the staff of the Muskogee General Hospital; aged 76; died, August 13, of cerebral hemorrhage.

Joseph R. Brown, Lavonia, Ga.; Georgia College of Eclectic Medicine and Surgery, Atlanta, 1899; member of the Medical Association of Georgia; aged 68; died, August 19, in a hospital at Atlanta, of pulmonary hemorrhage and bronchiectasis.

W. Clinton Linville * Goldsboro, N. C.; University of Maryland School of Medicine, Baltimore, 1903; at one time member of the state eugenics board; medical superintendent of the State Hospital; aged 59; died, August 30, of tuberculosis.

Eugene Monroe Allee, Speed, Mo.; Beaumont Hospital Medical College, St. Louis, 1892; member of the Missouri State Medical Association; also a druggist; formerly county coroner; aged 71; died, August 28, of cerebral hemorrhage.

Hugh L. Berry, Memphis, Tenn.; Vanderbilt University School of Medicine, Nashville, 1900; member of the Tennessee State Medical Association; aged 65; on the staff of St. Joseph's Hospital, where he died, August 23, of hypertensive heart disease.

Leonard Allen Baker * Middleboro, Mass.; Harvard University Medical School, Boston, 1905; formerly a member of the board of health; on the staff of St. Luke's Hospital; aged 57; died, August 8, in Boston of coronary heart disease.

Lewis Jones Blake * Spartanburg, S. C.; University of Pennsylvania Department of Medicine, Philadelphia, 1888; for many years president of the city board of health; aged 74; died, August 28, of myocarditis, cystitis and pyonephrosis.

Peter Hoffman Jr. ☉ Jersey City, N. J.; University of the City of New York Medical Department, 1882; for many years police physician; formerly on the staff of St. Francis Hospital; aged 77; died, August 1, of gastric carcinoma.

Granville B. O'Roark, Grayson, Ky.; Kentucky School of Medicine, Louisville, 1890; member of the Kentucky State Medical Association; on the staff of the J. Q. Stovall Memorial Hospital; aged 77; died, August 17, of heart disease.

Milton Morris Abeles, New York; University and Bellevue Hospital Medical College, New York, 1930; member of the psychiatric division of the Bellevue Hospital; aged 32; was killed, August 13, in an airplane accident in Germany.

Charles Edwin Blomgren ☉ Chicago; Rush Medical College, Chicago, 1899; on the staff of Augustana Hospital; aged 67; died, July 6, at his summer home in Lake Geneva, Wis., of coronary thrombosis and arteriosclerosis.

William Craw Gill, Cleveland; Western Reserve University Medical Department, Cleveland, 1900; veteran of the Spanish-American and World wars; aged 63; died, August 3, in St. Alexis Hospital of arthritis and arteriosclerosis.

Charles Wells Cropper, Jersey City, N. J.; Bellevue Hospital Medical College, New York, 1876; member of the Medical Society of the State of New Jersey; aged 90; died, August 8, of myocarditis and arteriosclerosis.

John Hampton Patton, Northport, Ala.; Maryland Medical College, Baltimore, 1902; member of the Medical Association of the State of Alabama; aged 59; died, in August, of injuries received in an automobile accident.

Norman Almon Burgess, Rock Creek, Ohio; Cleveland College of Physicians and Surgeons, Medical Department of Ohio Wesleyan University, 1904; aged 59; died, August 8, of hemiplegia, arteriosclerosis and nephritis.

Otis Little Cameron, Indian Hill, Ohio; Medical College of Ohio, Cincinnati, 1886; formerly county coroner and member of the board of health in Cincinnati; aged 76; died, August 21, of arteriosclerosis and angina pectoris.

Everett Allen Anderson, Georgetown, Ky.; Medical College of Ohio, Cincinnati, 1889; for many years connected with the United States Army; aged 71; died, August 31, of carcinoma of the lungs, liver and prostate.

Thomas E. Longshaw, Philadelphia; Jefferson Medical College of Philadelphia, 1901; member of the Medical Society of the State of Pennsylvania; aged 63; died, August 31, in Atlantic City, N. J., of acute myocarditis.

James Foster Merritt, Hot Springs National Park, Ark.; Dallas (Texas) Medical College, 1901; member of the Arkansas Medical Society; health officer; aged 69; died, August 11, of undulant fever and heat exhaustion.

Albert James Nute, Boston; Harvard University Medical School, Boston, 1902; at one time connected with the U. S. Public Health Service; served during the World War; aged 62; died, July 25, of heart disease.

Mary Elizabeth Jones, Boston; Woman's Medical College of the New York Infirmary for Women and Children, New York, 1890; aged 83; died, July 14, in the City Hospital of a hip fracture received in a fall.

Walter C. Palmer, Ranger, Texas; Columbian Medical College, Kansas City, Mo., 1899; formerly a pharmacist; served during the Spanish-American and World Wars; formerly health officer; aged 60; died, July 7.

William S. Lockert, Ashland City, Tenn. (licensed in Tennessee in 1898); county health officer; formerly member of the state legislature; aged 85; died, August 15, of uremia, arteriosclerosis and nephritis.

Ira Willis Ballard, Forest Park, Ga.; University of Alabama School of Medicine, University, 1919; member of the Medical Association of Georgia; aged 54; died, August 5, of streptococcal pneumonia.

Jonathan Shelton Hollis, Covin, Ala.; Medical College of Alabama, Mobile, 1884; member of the Medical Association of the State of Alabama; formerly member of the state legislature; aged 82; died, July 28.

Alfred Augustus Wheeler ☉ Leominster, Mass.; Harvard University Medical School, Boston, 1894; on the staff of the Leominster Hospital; aged 68; died, July 22, of carcinoma of the prostate.

Winston Churchill Crabtree ☉ San Diego, Calif.; University of Michigan Medical School, Ann Arbor, 1928; aged 36; died, July 14, in the Mercy Hospital of subacute bacterial endocarditis.

Frederick A. McWilliams, Monticello, N. Y.; Bellevue Hospital Medical College, New York, 1876; aged 85; died, July 20, in the Hamilton Avenue Hospital of chronic myocarditis.

Royal Wells Amidon, Chaumont, N. Y.; College of Physicians and Surgeons, Medical Department of Columbia College, New York, 1877; aged 84; died, July 8, of coronary thrombosis.

John Cotton Henry ☉ Athens, Ohio; Jefferson Medical College of Philadelphia, 1929; past president of the Athens County Medical Society; aged 34; died, August 9, of pneumonia.

Charles Dougald Black, Lansing, Mich.; Kansas City Homeopathic Medical College, 1891; at one time city physician and health officer; aged 85; died, August 19, of heart disease.

Warren Elsworth Danley ☉ Union City, Mich.; Northwestern Medical College, St. Joseph, Mo., 1889; formerly health officer; aged 73; died, August 10, of cerebral hemorrhage.

Edwin Louis Brown, Latta, S. C.; Medical College of South Carolina, Charleston, 1886; aged 79; died, August 11, in a hospital at Charlotte, N. C., of coronary occlusion.

Wilber J. James ☉ Excelsior Springs, Mo.; Eclectic Medical Institute, Cincinnati, 1894; aged 70; died, August 13, in the Excelsior Springs Sanitarium of bronchopneumonia.

Edwin Porter Linfield, Brockton, Mass.; Dartmouth Medical School, Hanover, N. H., 1879; member of the Massachusetts Medical Society; aged 82; died, July 24.

Oliver Joseph Miller, Sanford, Fla.; Jefferson Medical College of Philadelphia, 1905; aged 55; was found dead, August 3, of carbon monoxide poisoning self administered.

Gaylord McElroy Andrews, Auburn, Neb.; Marion-Sims College of Medicine, St. Louis, 1898; aged 67; died, July 1, in Minden of carcinoma of the mediastinum.

John Perry Martin ☉ Oakland, Calif.; California Medical College, San Francisco, 1903; aged 67; died, July 4, of chronic nephritis, heart disease and hypertension.

William Edwin Morgan, Philadelphia; Hahnemann Medical College and Hospital of Philadelphia, 1900; aged 59; died, July 26, of carcinoma of the pharynx.

Richard Henry Howard, Chicago; Meharry Medical College, Nashville, Tenn., 1916; aged 49; died, August 22, in the Provident Hospital of heart disease.

John Sorensen, Pasadena, Calif.; Københavns Universitet Laegevidenskabelige Fakultet, Denmark, 1892; aged 71; died, July 20, of pulmonary tuberculosis.

Charles Bell White, Walton, N. Y.; Bellevue Hospital Medical College, New York, 1883; aged 81; died, July 3, of a self-inflicted gunshot wound.

Edward Harvey Ellis, Marlboro, Mass.; Boston University School of Medicine, 1879; bank president; aged 81; died, August 2, of pneumonia.

Emily M. Luff, Oak Park, Ill.; Hahnemann Medical College and Hospital, Chicago, 1894; aged 75; died, August 6, of cerebral hemorrhage.

Moses Jacobson, Los Angeles; Cooper Medical College, San Francisco, 1901; aged 60; died, July 20, in the French Hospital.

Clarence L. Marlatt, Indianapolis; Central College of Physicians and Surgeons, Indianapolis, 1897; aged 63; died, July 31.

Benjamin Franklin Schofield, Fall River, Mass.; College of Physicians and Surgeons, Boston, 1896; aged 75; died, July 13.

William A. Webb, Lithonia, Ga.; Georgia College of Eclectic Medicine and Surgery, Atlanta, 1910; aged 63; died, July 2.

Reuben Nyswander, Grand Rapids, Ohio; Illinois Medical College, Chicago, 1904; aged 60; died, August 9, of heart disease.

Lafayette A. Craft, Herrick Center, Pa.; Eclectic Medical College of the City of New York, 1883; aged 80; died, July 19.

Ellen Bernadette Lysaght ☉ Brooklyn; Cornell University Medical College, New York, 1901; aged 63; died, July 31.

George Wesley Mixon, Hackleburg, Ala.; Medical College of Alabama, Mobile, 1904; aged 51; died, August 23.

Elbert Marion Myers, Bulls Gap, Tenn. (licensed in Tennessee in 1895); aged 67; died, August 4, of heart disease.

William Bradshaw Sharp, Hertford, N. C.; Leonard Medical School, Raleigh, 1901; aged 61; died, July 25.

Reese Edwin Reese, Fresno, Calif.; Cooper Medical College, San Francisco, 1895; aged 73; died, July 30.

Bureau of Investigation

IONITE

A Fraudulent "Consumption Cure"

Ionite was the trade-name of a "patent medicine" sold from Salt Lake City as a cure for tuberculosis. Five men were involved in the matter: (1) Jesse F. Barnhill, (2) James W. Morris, (3) Dean V. Johnson, (4) Asa L. Eddy and (5) Marcus Eddy. All five men were indicted on the charge of having used the United States mails in furtherance of a scheme to defraud. The two Eddys pleaded guilty; the other three went to trial. Morris and Johnson were acquitted; Barnhill was convicted and appealed. On April 12, 1938, the Circuit Court of Appeals, Tenth Circuit (Judges Phillips, Bratton and Williams), affirmed his conviction.

Barnhill seems to have been the king-pin of the cruel fraud. According to the testimony in the case he and Morris owned property in Nevada on which there was some clay. This clay was shipped to Salt Lake City and turned over to the Eddys, who had a drug store. Asa L. Eddy, the father of Marcus, was, according to information in the files of the Bureau of Investigation of the American Medical Association, a pharmacist who had previously owned a drug store. Marcus Eddy was not a registered pharmacist but, according to information received, had been a railway brakeman.

The Eddys took the clay shipped to them by Barnhill and proceeded to make a "consumption cure" out of it, by adding some "salts" to it, together with a small amount of potassium iodide, some glycerin, flavoring it with vanilla and sweetening it with saccharin. The finished product, according to Asa Eddy's testimony had the following composition:

Clay	20 pounds
Glauber's (horse) salts.....	8 pounds
Epsom salt	8 pounds
Potassium iodide	3 ounces
Glycerin	1 gallon
Water	5 gallons

This, according to Eddy's testimony made 108 bottles of "Ionite," each of which sold for Two Dollars (\$2.00)! At the time the post-office officials investigated the case 3,348 bottles had been sold.

Dean V. Johnson, although to the uninitiated apparently one of the chief factors in this swindle, seems to have been a stool-pigeon used by Barnhill as a "front." What, if anything, he got out of the fraud does not appear in the appellate court's review of the case. Long letters signed by Johnson were sent out on stationery bearing Johnson's name and address (Pleasant Grove, Utah) stating that he, Johnson, had been a sufferer from tuberculosis for some years and that the best efforts of physicians had completely failed to cure him. But after taking Ionite he claimed he was restored to normalcy! Accompanying the letter was an affidavit, also signed by Johnson, to the same general effect. It was brought out at the trial that Johnson was still tuberculous, and that whatever improvement he had shown was due to a pneumothorax performed by a reputable physician in a hospital. It was also proved that the letters and affidavits sent out in Johnson's name were dictated by Barnhill and sent out from Barnhill's office.

Nor was this all that stool-pigeon Johnson was used for. Large advertisements were published in the *Denver Post* in April, May and June 1935 all signed by Johnson and headed in large, black type: "ALL TUBERCULARS—NOTICE." These advertisements, in general, repeated the same fairy story about Johnson and his alleged experience with Ionite that appeared in the Johnson letters and affidavits. One of the advertisements was a vituperative attack on the medical profession in general and the American Medical Association in particular. The facts were that the advertisements were prepared and paid for by Barnhill, who admitted to post-office officials that he "paid for everything."

Two additional advertisements that appeared in the *Denver Post* in 1936 and 1937, respectively, were not signed by Johnson but appeared under the name of "Ionite Products." These are of interest in view of the fact that by May 1936 Johnson evi-

dently had lost faith in Ionite. For in that month he wrote a letter in which he admitted that he did not know of a cure for tuberculosis and advised his correspondent to go to the best physician he could afford. A month later—in June 1936—Johnson wrote another letter in which he admitted that he had tuberculosis!

Johnson was not the only stool-pigeon used by Barnhill in his fraudulent exploitation. Another affidavit was sent broadcast from Barnhill's office, signed "Mrs. Helene Greene." According to Mrs. Greene's affidavit she had a son, Delane, who for two years had suffered from tuberculosis and all efforts on his behalf by physicians had failed. But, Ionite had restored little Delane to perfect health. This affidavit was also dictated by Barnhill and when Barnhill's attorneys put Mrs. Greene on the stand she practically repudiated it although admitting that she signed it! She admitted that "the doctor did not say anything about her son having tuberculosis," nor had any x-ray examination ever been made, nor did she ever have her boy examined by "three specialists"—all of which the affidavit, signed by her but dictated by Barnhill, had affirmed.

During the trial a woman testified that having read the advertisements in the *Denver Post* she had ordered Ionite to give her tuberculous husband. The poor fellow took two bottles, got much worse and, some months later, died. Another witness, a man, testified that his tuberculous wife after reading the Johnson (Barnhill) advertisement in the *Denver Post* began taking Ionite and bought between 18 and 21 bottles. When she started taking Ionite she was walking around and doing her housework but soon began to lose weight until she had to go to a hospital. When the husband wrote asking for a refund he received no reply.

The Barnhill swindle, like many another consumption cure, worked the "refund" racket. The advertisements stated that if the purchasers were dissatisfied with the results the concern would refund the price of the first two bottles. In fact, this point was largely the basis of Barnhill's appeal, his attorneys arguing that the trial court erred in failing to instruct the jury as to the effect of a promise to refund the price, if made and carried out in good faith. This, too, in spite of the fact that Barnhill's attorneys at the trial made no request for such instruction. The Court of Appeals met the point admirably. Judge Williams, who wrote the decision, emphasized the fact that the "refund" was a most limited one; it applied only to the price of the first two bottles. Said the judge:

"It is highly probable that a man seriously affected with tuberculosis, and groping for a straw to save his mortal existence, for psychological reasons might reasonably at first be deceived into believing he was receiving benefits. Furthermore, it is likely that a person in such a condition of health would purchase more than two bottles and the refund offer might be considered a part of the scheme to induce such a person to get started in order to sell him many bottles of Ionite and make a nice profit even in face of a refund for two bottles."

The individuals found guilty of this cruel piece of medical fraud were actually small fry fakery. But what shall be said of a great metropolitan newspaper that accepted advertisements of such a fraud as Ionite and remained not only immune to any legal reprisals but seemed equally oblivious to any moral implications?

Medical Mythology.—Isis was the great goddess of medicine. It was she who gathered up the slain body of Osiris. Her sisters Nephthys and Neith were queens of the night and protected mortals from the pains that trouble them after dark. Sekhmet, the wife of the medical god Ptah, had the head of a lioness. She was the bone-setter and therapist, and saved from fire as well as from sickness. Bes, the smiling little god with a Mongolian face, presided over the birth house at the temples where the women were confined, and Hathor fed the infant and cured sterile mothers. Ubastet, Sekhmet's sister, was an obstetric goddess, and Meskenet had charge of the hot stones over which women crouched in labor.—Hurd-Mead, Kate Campbell: *A History of Women in Medicine*, Haddam, Conn., the Haddam Press, 1938.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

THERAPEUTIC MALARIA AND TRANSMISSION

To the Editor:—Frequently I use malaria inoculation for patients with dementia paralytica. 1. How soon after the inoculation can the mosquito carry their malarial infection to others? 2. How soon should they be put under screens? 3. What is the danger if they are allowed parole or visits? What difference is there in the activity of the mosquitoes between day and night?

M.D., California.

ANSWER.—1. Experience with inoculation malaria has shown that, following intravenous inoculation, *Plasmodium vivax* may be demonstrated in the blood of the recipient three days after the injection. In the majority of patients the plasmodium is present by the fourth or fifth day, usually from eighteen to thirty-six hours before the first chill.

2. The patient should be placed in a screened room immediately after inoculation, if all precautions to prevent dissemination of malaria are employed.

3. The danger of parole or visits during the incubation period lies in the (1) dissemination of malaria, (2) acquiring of intercurrent respiratory infections which may lead to pneumonia, (3) injudicious taking of drugs such as any of the coal tar products which may abort the malaria, and (4) development of inoculation chill and fever, which may appear from six to fifteen hours after the inoculation in patients who are mentally dull and which may lead to various complications as well as to misinterpretation of the chill.

The infected anopheles mosquito can transmit the plasmodium either during the day or during the night, but as this type of mosquito is a night feeder, it is more active during the night and the likelihood of transmission is greater, therefore, after sundown.

SCHNEIDER'S INDEX

To the Editor:—I should like a discussion of Schneider's index.

M.D., Illinois.

ANSWER.—In 1920 Edward C. Schneider of the Medical Research Laboratory, Air Service, Mitchel Field, Long Island, New York, published a paper entitled "A Cardiovascular Rating as a Measure of Physical Fatigue and Efficiency" (*THE JOURNAL* May 29, 1920, p. 1507), which proved to be of some value in weeding out the distinctly physically unfit among the individuals tested. He presented the plan in the first sentence of his paper: "The need of a measure for physical efficiency whereby degrees of fatigue, physical fitness and health may be determined has been felt alike by the medical profession and instructors in physical education and school hygiene." In the fifth paragraph he made the significant comment: "The cardiovascular changes during altered physical fitness have been studied most, and it is these that are considered in this paper. The tests here discussed should not be confused with functional heart tests. We are concerned with the cardiovascular changes only so far as they give evidence of fatigue and health changes in the body."

Toward the end of the paper he presented in detail the scheme of study which consisted of the determination of the heart rate reclining and standing, the number of beats the heart rate increases when the standing and reclining postures are compared, the acceleration in the pulse rate after exercise, the time taken by the pulse to return to normal and, lastly, the rise or fall in the systolic blood pressure on standing. A scoring system was used, based on these determinations. A perfect score was 18. For the details of the scoring the reader is referred to the original article by Schneider.

Schneider concluded: "That there may be value in assembling the circulation data under such a point system is indicated from an analysis of fifty-four cases of aviators who, when examined by the medical officers of the departments of the laboratory, were found to be ailing and physically below standard. . . . Only six of the fifty-four cases had a score of 10 or better, while 88.8 per cent had scores ranging between 9 and —1. These figures seem to indicate that a score of 9 or less is characteristic of physically unfit men."

A few years later F. S. Lee and J. D. Vanbuskirk (*Am. J. Physiol.* 63:185 [Jan.] 1923) tried out Schneider's test in the case of a professor and three undergraduate students to determine the effect of unusual physical exercise; a walk of about fourteen miles a day on several work days, interspersed with rest days. They were unable to find that Schneider's test was a reliable criterion of daily physical fatigue, although it might have "value in the detection of pronounced physical deterioration amounting often to a pathological condition, or of fatigue masses."

Thus it would seem that Schneider's test of physical fitness, like many others, must be interpreted with considerable caution. When, however, a distinctly low rating is obtained it is almost certain that the individual being tested is in poor condition. Under such circumstances the poor physical condition may be obvious without the test; but still the test gives something of a quantitative measurement and so may be of some use.

ABSORPTION FROM URINARY BLADDER

To the Editor:—Has any work been done or anything published relative to the capacity of the human bladder to concentrate urine? From clinical observation and some crude experimentation I believe it is possible that water can be resorbed from the urine in maintaining the water balance of the tissues, which to my knowledge has never been ascribed to it. I have never seen anything in the literature pertaining to this subject and have always seen the bladder described as merely a reservoir and nothing else. If any work has been published relative to this or the idea proposed will you inform me?

M.D., Connecticut.

ANSWER.—The possibility of absorption from the urinary bladder has been considered by many observers and a great variety of experiments have been made to determine the degree of absorption. A review of this work is included, with a list of references, in a paper written by Mann and Magoun entitled "Absorption from the Urinary Bladder" (*Am. J. M. Sc.* 166:95 [July] 1923). Using phenolsulfonphthalein as the test substance in a series of experiments, they came to the conclusion that when the dye was placed in the urinary bladder it appeared in the excreted urine in relatively small amounts. They concluded that, while absorption undoubtedly takes place from the urinary bladder, it occurs to such a limited extent that it has little or no practical significance.

These deductions are corroborated by the work of Vickers and Marshall in a paper entitled "Permeability of the Urinary Bladder to Urea and Sodium Chloride" (*Am. J. Physiol.* 70:40 [Nov.] 1924). They concluded from their experiments that urea and sodium chloride are possibly absorbed from the bladder but only to a slight degree. Although they did not attempt to estimate to what extent water is reabsorbed, they were under the impression that it could concentrate the urine but little.

OPERATIONS FOR STERILITY IN WOMEN

To the Editor:—A woman aged 36 wants to become pregnant. She had both fallopian tubes resected three years ago. Before this she had two pregnancies terminated by induced abortions due to severe vomiting. I am writing to ask whether surgical treatment would be advisable in order to allow her to become pregnant again. What are the chances of success in her becoming pregnant and in her going to full term? What is the nature of this operation and what are the associated duties involved once she has become pregnant?

M. D., New York.

ANSWER.—Since the patient does not possess either fallopian tube, the choice of operation which may lead to a pregnancy lies between implantation of one ovary inside the uterine cavity and implantation of half an ovary on one or both corners of the uterus. The insertion of an ovary inside the uterine cavity has few adherents because the chances of having a baby after it are remote and there are too many associated complications. On the other hand, the operation of implantation of a part of an ovary on the uterine cornua, known as the Estes operation, is followed by a small percentage of successes.

Von Graff (*Iowa State J. Med.* 26:31 [Jan.] 1936) collected sixty-six cases in which a graft of ovarian tissue was placed on a uterine horn or on a tubal stump. He reported fourteen pregnancies (21.2 per cent) following these operations. However, since only five of these pregnancies went to term, only 7.6 per cent of the operations, or one in 13.2 operations, resulted in a full-term baby. Among the remaining nine gestations there were six abortions and one ectopic pregnancy. The cause in two cases was unknown. In von Graff's collected series of forty-one cases in which an ovary was transplanted into the uterine cavity, only three pregnancies (7.5 per cent) resulted, of which one went to term (2.4 per cent) and the other two ended in abortion. Reiprich (*Ztschr. f. Geburtsh.* 2:

Gynäk. 104:1 [No. 1] 1932) collected 200 ovarian transplants of all types and reported only five pregnancies (2.5 per cent) following these operations. Estes (*Surg., Gynec. & Obst.* 38:394 [March] 1924) followed up twenty-seven of eighty-eight patients on whom he had performed his ovarian transplantation operation and found that pregnancy had occurred in four of them (15 per cent). In a later article, Estes (*Am. J. Surg.* 24:563 [June] 1934) reported that, in a series of fifty patients whose case records were complete, only four became pregnant (8 per cent). Two of these women had abortions and two had full-term babies.

Sovak (quoted by Greenhill: *Am. J. Obst. & Gynec.* 33:39 [Jan.] 1937) states that four pregnancies resulted after the six Estes operations he performed. Three of these women had induced abortions but the fourth patient had a spontaneous abortion.

Should an operation be performed to overcome this patient's sterility and should a pregnancy follow, the patient will have to be watched closely during pregnancy and particularly in labor. Serious complications have occurred after these operations just as they have taken place after plastic operations on the fallopian tubes to overcome sterility.

EARLY HAY FEVER—COSEASONAL TREATMENT

To the Editor.—From August 4 to 11 I had three patients who started having hay fever earlier than usual. Please give a list of the flowers that pollinate in New England at this time. Is there any possibility that the unusual wet weather has caused some ragweed to pollinate early? Please outline a tentative series of ragweed injections to be given now to a man 38 years of age who is already having a vaccine composed of various bacteria to which he is skin positive and which apparently causes a severe asthma in the winter. He is one of the patients who has reactions to ragweed but has already begun to have severe attacks of sneezing.

OLIVER S. HAYWARD, M.D., New London, N. H.

ANSWER.—The ragweed hay fever season started earlier in sections where there had been considerable rainfall. There was a fair amount of pollen in the air in some sections, August 5. In New England as in most of the northern and central parts of the United States the ragweed constitutes the main cause of hay fever at this time of year. It is possible, of course, that this particular patient was extremely sensitive and hence had symptoms early. In addition, sometimes handling flowers of composite families brings on symptoms early.

The best method of coseasonal ragweed therapy consists of giving intradermally weak extracts of ragweed pollen, beginning with about 5 units and increasing slowly every day or every other day. After the season is over, the injections should be given subcutaneously about once every two weeks with the usual increases of from 25 to 50 per cent. No increase should be given if there is any considerable reaction.

SUBLUXATION OF SACRO-ILIAC—DISABILITY

To the Editor.—A man aged 40 sustained a severe trauma which resulted in a right sacro-iliac subluxation. In spite of treatment the joint remained after nine months painful and extremely tender to deep palpation along the site of the joint, and the patient is unable to bear full weight on the right leg without limping and severe pain. Will this ever return to normal so that he can do heavy laboring work without recurrence of symptoms so severe as to force him to discontinue? Is he permanently and totally disabled for pursuing his occupation of hard labor? What is the prognosis for ultimate cure?

DAVID KRAMER, M.D., Silver City, N. M.

ANSWER.—To answer this query one should have additional information. Treatment which has been carried out for the patient is not mentioned. It would be of some help to know whether or not the pain has been localized to the sacro-iliac joint or has radiated along the course of the sciatic nerve. Most injuries of the type referred to heal, with complete restoration of function, if the back is adequately protected for a sufficiently long time. If subluxation can be definitely established, either by clinical examination or by roentgenographic studies, manipulation should be carried out with the patient fully relaxed by a general anesthetic. This manipulation consists principally of forced flexion of the thigh, with the knee completely extended, and abduction and hyperextension of the thigh at the hip. In view of the fact that the patient has been disabled for nine months, a bilateral body and leg cast should be applied after the manipulation and worn for three weeks. The cast should then be bivalved and the patient given daily heat and massage to the low back region. In addition the physical therapist should teach the patient exercises for contracting and strengthening the abdominal and the gluteal muscles. Six weeks from the date this program of treatment is begun, the patient may be

allowed up wearing a back brace. Activity should be stopped short of fatigue or recurrence of the pain. If this program is followed, functional recovery may be anticipated approximately three months from the date of beginning treatment. The back brace should be worn for a full year as a safeguard against recurrent attacks of the pain. A few of the patients with low back injuries of the type described may not respond to the treatment outlined. These patients are entitled to the benefit of an arthrodesis operation on the joint affected.

Orthopedic procedures such as those described should afford a favorable prognosis so that the patient may eventually do heavy laboring work. He should not be permanently and totally disabled from pursuing an occupation of hard labor. The prognosis for ultimate cure depends largely on the type of treatment and the thoroughness with which it is carried out.

SPEECH DEFECTS IN FAMILY

To the Editor.—In a family of three boys and five girls of healthy parentage, with no history of syphilis or nervous diseases, the boys have defective speech which consists of inability to enunciate certain words or parts of words containing certain combinations of letters. For example, they say "trotlight" for spotlight, "you" for you, "houshe" for house. The defect is generally known as tongue-tie. However, the frenum of the tongue is normal and there is no malformation or defect in any part of the vocal apparatus. The males of the family are all intelligent and successful business men, two of them being married and having children. One of these men, married to a healthy mate, has three children: one girl, who talks well; a boy aged 5 who is apparently above the average in intelligence but who shows the same defects that his father has in speaking, and a younger boy not old enough for abnormality of speech to be detected. Is this a hereditary defect? Why does it appear in the males and not in the females? Beginning in the formative stage of life, could this defect be overcome by intelligent home training by a patient and persevering mother? Are there any institutions devoting special attention to correction of speech defects located in this or near by states? Please refer to any available literature on this subject, especially that bearing on home training for correction of defective speech. The father does not want his son to go through life handicapped as he is. M. D., Georgia.

ANSWER.—The problem of the influence of heredity on speech defects is still uncertain. Some speech deficiencies certainly run in families, but one cannot eliminate the influence of mimicry by children when they hear a parent manifesting a speech defect. There is furthermore no relationship between intelligence and the speech defect, so that the fact that some of the males in the family are successful business men and also the fact that the men have a defect and not the girls is not at all unusual, for where there is a disorder which is of hereditary origin, such as color blindness and hemophilia, it is not uncommon to find sex linking, whereby the females of the family carry the trait but do not manifest it, whereas the males manifest it and do not necessarily pass it on to their children. However, one would not judge from the degree of this type of defect that it is likely to be truly hereditary in origin because mispronunciation of words in a characteristic fashion is too complex to follow the usual genetic pattern that one would expect. In cases of speech difficulty training seems to be the most promising approach, and certainly the earlier the training is undertaken the more promising the therapy becomes. Mere drill sometimes is useful, and if the physician is too far away from a large university where there is a special department of speech analysis and correction he may attempt to do this with the younger members of the family. However, the psychologic and physical problems in the dynamics of speech are so complicated that it would seem dubious whether the physician could justify himself in making a thorough study of the whole problem in particular reference to a case, and it would probably serve his patients better, or at least the younger members of the family, to get in touch with a highly specialized department of speech difficulty, like the departments at Northwestern University or the University of Michigan. Definite speech clinics do not seem to be prevalent, at least in the South, but assistance might be obtained from the director of the Family Welfare Society Mental Hygiene Clinic in Atlanta, or the Grady Hospital Neuropsychiatric Clinic in that city. As far as literature is concerned, it is vast and conglomerate, but the following might be referred to:

Twitmer, Edwin B., and Nathanson, Yale S.: *Correction of Speech Defects*, Philadelphia, P. Blakiston's Son & Co., 1932.

Travis, Lee E.: *Speech Pathology*, New York, D. Appleton-Century Company, 1931.

Stinchfield, S. M.: *Speech Disorders*, New York, Harcourt, Brace & Co., 1933.

West, R. W.: *Disorders of Speech and Voice*, Madison, Wis., College Typing Company, 1935.

Diagnosis of Disorders of Speech, 1936.

Blanton, Margaret Gray, and Blanton, Smiley: *Speech Training for Children: The Hygiene of Speech*, New York, Century Company, 1919 (this older volume is not considered up to date).

PRECOCIOUS MENSTRUATION

To the Editor:—I have a patient who is unique so far as my thirty years' general practice is concerned. This girl, just a little over 2 years of age, has been menstruating lightly for several months, but for the last three months she has menstruated more freely at regular intervals. Otherwise she is a normal child. Please advise possible cause, treatment and prognosis.

P. M. RICHARDSON, M.D., Cushing, Okla.

ANSWER.—Children may show signs of premature menstruation or precocious maturity when there is no discoverable cause. In those instances in which the menstrual flow takes place at more or less regular intervals, secondary manifestations of sexual and somatic precocity may occur, although such cases have not been frequently recorded. Some of these little girls continue to menstruate for a certain period and then the flow stops entirely. Others have been observed to continue until the usual menstrual period.

A form of menstruation sometimes occurs in newborn babies, though in these cases the bloody discharge is usually small in amount and lasts only a short time. It has been thought that it bears some relationship to endocrine products of the placenta, and its cause may be compared with the enlargement of the breasts in newborn infants. Cases have been reported in which precocious menstruation has occurred as a result of ovarian tumor, though in this connection it should be recalled that numerous patients have been observed with ovarian tumors without premature sexual development or precocious menstruation. R. T. Frank recovered female sex hormones in the urine during the menstrual period of a girl 3 years of age. He concludes that, if the hormone is present in the urine, it indicates an ovarian tumor.

Precocious puberty in girls may also be the result of hypersecretion of the anterior lobe of the pituitary gland. In little girls of this type, mental development is slow and they tend to show excessive growth and increased sexuality.

The treatment depends on the underlying cause. The child should be kept under observation until the diagnosis is established. Little or nothing is to be expected from endocrine treatment in these cases.

The parents should be warned that, on account of premature sex development, impregnation may occur. In a case reported by Haller, menstruation began at 2 and a pregnancy occurred at 8 years of age.

POSSIBLE DANGERS FROM BOILER CLEANER

To the Editor:—Might there be deleterious effects on the health of enrollees as a result of the use in CCC camps of a boiler cleaning compound known as Industrial Boiler Water Treatment, manufactured by the Industrial Products Company, St. Joseph, Mo.

OSCAR D. GROSHART, M.D., Fort Worth, Texas.

ANSWER.—This inquiry does not furnish statements with reference to the conditions of water use from which injury might be anticipated; that is, through water drinking or bathing, or from the manipulation of chemicals used in water treatment. For this reason the reply made is general and is without reference to any one particular product. The number of substances that are used in boiler treatment is legion and include sodium silicate, caustic soda, soda ash, trisodium phosphate, disodium phosphate, potassium salts, acetic acid, sodium phosphate, lime soda, calcium hydroxide, sodium aluminate, phosphoric acid, hydrochloric acid, zeolites (which are complex silicates of aluminum and alkali metals), cyanides, ferrous sulfate, sodium bicarbonate, tannic acid, gum catechu, hemlock bark extract, cactus juice, starches and fats. Almost any of these substances brought directly in contact with the skin might produce a dermatitis, so that boiler room workers are those most likely to be affected. Whenever other persons are damaged, this usually results from the misapplication of chemicals, and particularly the use of treated waters without due regard for the necessity of boiler and pipe flushing. Since fairly large amounts of some of these chemicals may be used in scale removal from boilers and pipes, it becomes clearly possible that negligence in thoroughly removing all these chemicals might lead to widespread injury to persons consuming the water and particularly in a restricted water system such as in a small camp. One consideration in this situation is with respect to the solution of lead in lead pipes and lead compounds that have been applied to pipe joints. The presence of appreciable quantities of carbon dioxide in water may distinctly influence the solubility of lead that may be present. In times past, soda water fountains extensively used lead pipes through which carbonated water passed until it was discovered that a possible lead exposure was thus

introduced. The chemical content of a water supply prior to its introduction into boilers stands in some relation to the action of cleaning agents and the possibility of ensuing injury.

In some instances boiler water supplies are continuously treated with chemicals, use being made of practices not used by those employed in the softening of waters by municipalities for general household use. Particularly, this process, when properly applied, is unlikely to lead to damage. So many factors may influence the possibility of injury under the circumstances mentioned that in any one given instance it is not practical to make precise claims. In the present instance the water should be analyzed for lead, chromates, acidity or alkalinity from samples taken at times and places most likely to be associated with injury.

SIMULTANEOUS ADMINISTRATION OF DIGITALIS AND THEOCALCIN

To the Editor:—Based apparently on the reports of death following intravenous administration of calcium in patients receiving digitalis, certain physicians in this vicinity are of the opinion that it is dangerous to give theocalcin and digitalis at the same time to cardiac patients. I am of the opinion that the calcium present in the theocalcin tablet is not so great as such and that there is no danger of a cardiac standstill resulting from the use of the two drugs. Please discuss this problem.

M. D., Arkansas

ANSWER.—It is improbable that digitalis and theocalcin given at the same time in therapeutic doses will produce any untoward results. This combination has been given thousands of times and no report of unfavorable action has been found in the literature. Theocalcin is calcium theobromine with calcium salicylate. It contains about 10 per cent of calcium. The average dose of theocalcin by mouth (it is impossible to give it any other way) is 2 Gm. (30 grains) daily in divided doses. This dose contains about 0.2 Gm. (3 grains) of calcium. The largest recommended dose of 5 Gm. (75 to 80 grains) daily contains about 0.5 Gm. (8 grains) of calcium. It is doubtful that such amounts given by the oral route in divided doses will produce any effect on the blood calcium level. In the cases of sudden death reported by Bower and Mengle, calcium was given intravenously. In the experimental work concerning digitalis and calcium, the calcium was likewise given intravenously. In the experimental work showing the effect of calcium on the heart muscle the calcium was introduced intravenously or by perfusion. In such instances there will be an appreciable elevation of the blood calcium, and the calcium enters the heart muscle almost immediately. In the case of theocalcin the calcium is absorbed slowly from the gastrointestinal tract, passing through other organs before reaching the heart, and indeed it seems likely that some of it is precipitated in the intestinal tract in the form of insoluble salts and is not absorbed at all. The theobromine is the active ingredient. Neither reason nor experience points to any contraindication to the simultaneous use of these drugs.

SINUSITIS AND BACTEREMIA

To the Editor:—I would greatly appreciate some information concerning the incidence of pneumococcal and other bacteremias following the complicated and uncomplicated nasal sinusitis. References to the literature would be appreciated.

SAUL SOLOMON, M.D., New York

ANSWER.—Not much work has been done concerning the incidence of bacteremias following sinusitis. Bacteremia in the presence of uncomplicated sinusitis occurs rarely if at all, even though the febrile reaction is severe. In the series reported by Goldman of complications following sinusitis positive blood cultures were obtained in 44 per cent of the cases in which this test was done, and it was felt that this percentage would have been even higher if more than one culture had been taken on each patient.

The possibility of a bacteremia depends not only on the presence of a complication but also on the variety. Thus it is most likely in cavernous sinus thrombosis; it occurs in a high percentage of cases of meningitis, orbital abscess and osteomyelitis of the skull and is less common in brain abscess and orbital cellulitis.

Of sixteen bacteremias Goldman found *Streptococcus hemolyticus* in eleven cases, *pneumococcus* type III in two cases, *pneumococcus* type I in one case, *pneumococcus* type XXI in one case and *Staphylococcus aureus* in one case.

As a rule the occurrence of a positive blood culture in acute sinusitis points to the coexistence of a complication or some associated systemic disorder. Of course, it is open to question

whether the bacteremia is dependent on the severe sinusitis which causes the complication or whether the blood stream invasion is from the secondary focus.

Larsell, Veazie and Fenton, working experimentally with cats and rabbits whose sinuses and draining lymph nodes they inoculated with hemolytic streptococci, recovered the organism from the heart's blood, spleen and liver, thus showing conclusively that there was a hematogenous phase to the infection, the route being the pretracheal lymphatic vessels to the great veins and then into the right side of the heart and into the pulmonary capillary bed. However, it appears even in this experimental work that the blood stream is pretty well cleared of organisms in about twenty-four hours, the lymph nodes draining the sinuses, the lungs, the spleen and the Kupffer cells of the liver acting as filters.

References:

- Goldman, J. S., and Schwartzman, Gregory: *Ann. Otol., Rhin. & Laryng.* 44: 961 (Dec.) 1935.
Goldman, J. L.: *Laryngoscope* 46: 500 (July) 1936.
Larsell, Olof; Veazie, Lyle, and Fenton, R. A.: Streptococcal Infection of the Lungs from the Paranasal Sinuses, *Arch. Otolaryng.* 27: 143 (Feb.) 1938.

DEATH FOLLOWING BLOW OVER LARYNX

To the Editor:—Recently I was called on to make a postmortem examination of a white man aged 28 who had been in a brawl and who, according to reports, had received one blow on the side of the face and a second about one inch below the larynx. Following this he was reported to have dropped dead. My examination gave essentially negative results except for bruises on the face and lips and a small bruise over the trachea in the spot before mentioned. There was no hemorrhage in this area except a small spot under the skin. There were no fractures of the laryngeal cartilages or of the tracheal rings and there was no gross edema. There was no cord injury. Would it be possible for a blow in this area to cause death? If so, please explain the mechanism involved.

M.D., Indiana.

ANSWER.—Deaths have been reported following single sudden blows on the larynx or trachea. They have been explained as arising from pressure on the carotid sinus or from insult to the vagus nerve, causing reflex cardiac paralysis. In most cases, in young persons with no cerebral or cardiac disease, the victim has been profoundly alcoholic. However, these cases are so rare and the explanation so theoretical that the observations are looked on with suspicion. Continued pressure on the larynx or trachea may produce asphyxial death, leaving little or no local evidence.

TREATMENT OF HEMANGIOMA IN INFANTS

To the Editor:—Please give the proper technic of using carbon dioxide snow or dry ice in the removal of a hemangioma which is just starting to grow on the abdomen of a baby 6 months old.

HARRY C. BARBER, M.D., Normal, Ill.

To the Editor:—I have been informed that the treatment of small hemangiomas of the skin of children is best accomplished either by radium or by carbon dioxide snow. What is the technic of using carbon dioxide snow? Would not freezing by means of ethyl chloride, which seems so much simpler, be satisfactory? One patient has a growing hemangioma of the scalp partly overlying the anterior fontanel. The patient is 7 weeks old. Would treatment endanger the sagittal sinus?

M.D., Montana.

ANSWER.—Freezing the skin by means of ethyl chloride for a brief period does not cause destruction of the skin. It does not compare with carbon dioxide snow in its ability to lower temperature and it is impossible to use pressure with ethyl chloride as with the snow. Without pressure a layer of gas forms below the snow and protects the skin, preventing adequate freezing for the purpose desired.

The snow is obtained by releasing liquid carbon dioxide into a chamois skin folded to make a bag. The sudden lessening of pressure allows the liquid to turn to the gaseous form so quickly that a great deal of heat is rendered latent and a small amount of liquid carbon dioxide is frozen. This snow is collected in a cylinder of the desired size and packed down by a ramrod. The warmth of the hand loosens the pencil of snow and it is removed from the cylinder and shaped on a flat surface of a heavy metal object like a flat iron. When of the right shape, it is pressed firmly on the lesion for from three to fifteen seconds, seldom longer in a baby, whose skin reacts more readily than that of an adult. The hair must be shaved from the scalp to get good apposition. Over a foundation of bone it is much easier to maintain pressure than on a soft surface as over the fontanel. It is not likely that there will be any injury to the sinus, for the effect of snow in this dosage is superficial. The fears of the mother must be considered, however. In treating a baby it is well to begin with a minimal dose and lengthen

the time of freezing until sufficient to cause a bleb. This will probably burst and should be kept as clean as possible, by cleansing with hydrogen peroxide and dressing with sterile boric petrolatum. After healing the treatment can be repeated if thought advisable. Better results, with less scarring, are obtained from repeated small doses rather than a few large ones.

If the angioma is cavernous, radium treatment is preferred.

MYOTONIA CONGENITA (THOMSEN'S DISEASE)

To the Editor:—What is the treatment for myotonia congenita (Thomsen's disease)? In our hospital quinine hydrochloride is used for symptoms, but my case requires a minimum daily dose of 1 Gm. and the resulting tinnitus is worse than the disease. What is the etiology? Is it an endocrine or potassium-calcium imbalance or excess of acetylcholine?

ARTHUR GAEBLER, M.D., Illinois.

ANSWER.—Myotonia congenita (Thomsen's disease) is at present considered to be a disease of the muscle or myoneural junction. The etiology is unknown. Quinine is thought to be effective by destroying or preventing the action of the vagus stuff at the myoneural junction. In this respect it is supposed to act in a manner opposite to prostigmine in myasthenia gravis. In some cases there may be endocrine factors. This aspect should be investigated and if found the factors should be corrected.

Quinine hydrochloride is usually well tolerated by these patients. It may be well to try to establish tolerance with a total daily dose of 0.3 Gm. and then gradually increase the dose to the point at which the symptoms are controlled.

CHRONIC GONORRHEAL URETHRITIS

To the Editor:—A patient who has had a chronic posterior gonorrheal urethritis for many years has had about everything that has ever been utilized in the treatment of this condition. He has had several recurrences. In spite of weekly prostatic massages and the use of sounds for the past few months he continues to have a tickling sensation in the meatus. The latter symptom improved for a while after I began using sounds but it recurred a few weeks ago. Not knowing what else might be done for him, I am wondering whether sulfanilamide, which has been recommended so highly for a variety of infectious processes, might not be used. What dosage of sulfanilamide is given the first day or two, how much daily the rest of the time, how long should it be continued and should alkali be given with it?

M.D., Illinois.

ANSWER.—The presence of a tickling sensation in the meatus in the course of a chronic gonorrheal urethritis may be due to a narrowing of the meatus, a soft or hard urethral infiltration, a verumontanitis, granulation of the posterior urethra or a persistent prostatitis.

It may be necessary to do a small meatotomy to enlarge the meatus. The urethral caliber varies, but at least a No. 25 F. should be taken. Urethroscopy is indicated to ascertain a lesion of the verumontanum, which, if found, may be treated with increasing strengths of silver nitrate, beginning with a 1 per cent solution.

Prostatovesiculitis must be treated by massage and local instillation as well as by chemotherapy. It is best not to massage more often than one or two times a week.

The use of sulfanilamide in these cases is frequently of value. Dosage varies with age and general condition. The average ambulatory male will tolerate 2.6 Gm. (40 grains) a day for two or three days, with gradually decreasing dosage for a period of from two to three weeks only. Sodium bicarbonate 2.6 Gm. a day should be given with the sulfanilamide for the entire course of treatment. It is important to give no other medication with these drugs. Saline cathartics are especially contra-indicated.

IMMUNITY IN GONORRHEA

To the Editor:—I should like information on immunology in its relation to gonorrhea.

JOSEPH N. SEGAL, M.D., Boston.

ANSWER.—There is little known at the present time about immunity and its relation to gonorrhea. Beyond any doubt some patients when infected with this organism will have a mild form of the disease and others will have a severe form. Experimentally it has been shown that the virulence of the numerous strains of gonococci varies greatly. This has been adequately tested as regards the thermal death point of the various strains. Clinically these facts are again brought out. Individuals known to be infected with the same organism usually respond in a similar way to treatment. No doubt personal immunity does play some part in gonorrhea but it seems to be slight.

TIME OF CIRCUMCISION—COAGULATION TIME IN NEWBORN

To the Editor:—What is the optimum time for circumcision of a newborn baby? Is the coagulation of the blood greater at birth than a few hours or a day or so later? If so, please give references to the literature.

M.D., Kentucky.

ANSWER.—According to the ancient custom, circumcision was performed on the eighth day after birth, though some tribes performed the rite at the second week. According to the custom of the present day, the operation is usually performed at the end of the first week after birth but is sometimes deferred to a week or ten days later.

The coagulation time of the blood in the newborn is prolonged for the first days of life, after which there is a decrease in the coagulation time, which reaches a level about the tenth day of life. At birth the coagulation time is nearly always at about the normal adult level but is prolonged somewhat in the presence of icterus. The greatest increase in coagulation time is noted on the third day of life.

References:

- Lucas, W. P.; Dearing, B. F.; Hoobler, H. R.; Cox, Anita; Jones, Martha R., and Smyth, F. C.: Blood Studies in the Newborn, *Am. J. Dis. Child.* 22: 525 (Dec.) 1921.
Rodda, F. C.: Studies with a New Method for Determining the Coagulation Time of the Blood in the Newborn, *ibid.* 19: 269 (April) 1920.

SODIUM BICARBONATE DEPOSIT ON STERILIZER

To the Editor:—Without my knowledge my nurse had been placing a drachm of sodium bicarbonate in my sterilizer each day for several months, thinking that it prevented rust. Of course, this has affected all my syringes. We have thoroughly washed and scrubbed the sterilizer daily and have at times placed large amounts of boric acid solution in the sterilizer in an attempt to remove the remaining portion of sodium bicarbonate, but all this has been in vain. The syringes are always covered with a thin film of the powder as well as the sterilizer following drainage. Can you suggest other means of removing the powder?

M.D., Virginia.

ANSWER.—Washing in large amounts of distilled water should remove both the sodium bicarbonate and the boric acid from the sterilizer. However, a 1 per cent hydrochloric acid solution followed by rinsing well with distilled water should remove all traces of the sodium bicarbonate. This should be used with care in metal sterilizers. It is possible that the thin film on the syringes and sterilizer is salts from tap water and is not sodium bicarbonate.

BITTER SKIN FROM DRUGS?

To the Editor:—Will theobromine cause bitterness of skin and finger-nails when taken over a period of time? My patient has also been taking digitalis and a salicylic acid compound. Would either of these drugs be a possible causative agent? If none of these drugs cause this symptom, what are some other possibilities?

M.D., Ohio.

ANSWER.—There is a possibility of dermal elimination of substances, such as alkaloids, although the matter has not been extensively investigated. Stockman in 1906 (*Edinburgh M. J.* 2:103, 1906) found traces of salicyl in the sweat and Vinci (*Biochem. Zentralbl.* 4:240, 1905) found salicyl in all organs and secretions; salicylic acid per se does not exist in tissues; buffer action prevents its occurrence as an acid. The condition of the skin may, of course, be due to elimination of the sweat of endogenously produced bodies and it may be well to investigate the condition of the kidney and of the alimentary tract if the condition persists in spite of discontinuance of the medicine.

SEPTIC TANK AND SURVIVAL OF BACTERIA

To the Editor:—I am planning a cabin in the north woods on an island. I should like information on the efficacy of a septic tank in relation to contamination of drinking water obtained from deep down in the Lake of the Woods approximately fifty feet from shore. I understand that if the liquid draining from the septic tanks is distributed under ground over a reasonably large area the bacteria contained become killed. Any information will be appreciated.

M.D., Illinois.

ANSWER.—It is not definitely known how rapidly pathogenic bacteria disappear in a septic tank. Although it is probable that these organisms do not survive any great length of time, they may appear in the effluent, particularly if circulation in the tank is relatively rapid. The movement of fecal pollution in ground water has been studied, with *B. coli* and the dye uranin used as indicators (Stiles, C. W., and Crohurst, H. R.: *Pub. Health Rep.* 38:1350 [June 15] 1923). Pollution was found to penetrate a fine sandy soil for 115 feet in 187 days. The distance to which pollution may so penetrate is dependent on a

number of interrelated factors, the most important of which are the ground formation, wet and dry weather with resulting rise and fall of the ground water level, the length of the wet and dry periods, the viability of the bacteria under the conditions of moisture, food supply and pH that may obtain. Laboratory experiments indicate that the typhoid bacillus may survive two or three weeks in unsterilized ground water.

EFFECT OF IODINE FUMES ON SKIN

To the Editor:—A man in Los Angeles is enthusiastic over a vaporizer in which he uses iodine crystals and sprays the fumes daily on the skin or other involved portions of the body, claiming that the iodine thus applied has a therapeutic effect not otherwise obtained. He advocates its use in carbuncles, boils, sore throat, acne and vaginitis. Is there any proved worth or merit in such a procedure?

M.D., Los Angeles.

ANSWER.—No. There is no possibility that the iodine fumes could have better effect than that which would be obtained when applied to the skin in equivalent concentration by other means.

ALUM IN DIPHTHERIA TOXOID

To the Editor:—Can you advise me of any diseases in which alum is given hypodermically? What would be the effects and what is the amount each patient receives that is given a dose of diphtheria toxin alum precipitated?

C. W. BESON, M.D., Oklahoma City.

ANSWER.—The quantity of alum in diphtheria toxoid alum precipitated does not exceed 20 mg. per dose. There is no likelihood that alum given hypodermically would be of any value in any disease. It would certainly be destructive to the subcutaneous tissue if employed in any considerable concentration. This is due to its protein precipitant quality, which is absent when it is used in diphtheria toxoid as the protein precipitant action has been neutralized in the formation of this product.

X-RAYS AND RADIUM IN MENORRHAGIA

To the Editor:—What effect will 100 mg. of radium applied to the uterus for six hours, or the equivalent of x-rays, have on the sexual desire and orgasm in a woman 35 years of age? Which would be better, radium or x-rays, to control menorrhagia (not pathologic but probably due to hypochromic anemia)?

M.D., Louisiana.

ANSWER.—There is every reason to believe that the insertion of 100 mg. of radium in the uterus for six hours in a woman 35 years of age has no effect on sexual desire and orgasm. There is little choice between the use of x-rays and radium in equivalent doses for the control of functional menorrhagia.

OBESITY AND HYPERTENSION—RACIAL INCIDENCE

To the Editor:—1. Is there any proved relationship between obesity and hypertension? 2. In this country is there a racial difference in the incidence of hypertension?

M.D., Missouri.

ANSWER.—1. There is no proved etiologic relationship between obesity and hypertension, although at one time such was the general opinion. Hypertensive arterial disease and diabetes mellitus of the late type are, however, encountered frequently in the same individuals. This coexistence of the two diseases is more common among obese persons with diabetes. Obesity affects the prognosis in hypertensive disease adversely. There is greater cardiac strain and likelihood of earlier renal depreciation.

2. There are no well defined racial differences in the incidence of hypertensive disease. As this disorder is an exceptionally variable one and each case is individual, it is difficult and precarious to indulge in generalizations.

EXCESS HAIR OF CHEST

To the Editor:—A patient is desirous of removing thick matted hair covering more than three fourths of his chest. He is much embarrassed by this extreme hirsutism and has asked me as to the advisability of careful x-ray exposure or any other remedy.

M.D., New York.

ANSWER.—There is no safe way of permanently removing hair. Without any question hair can be removed by x-rays but it is not a safe procedure at the present time to attempt to remove hair permanently by this means. There are various mechanical and chemical methods of removing hair temporarily but there are none which can be advised as thoroughly safe or permanent.

Medical Examinations and Licensure

COMING EXAMINATIONS

STATE AND TERRITORIAL BDARDS

ALABAMA: Montgomery, Jan. 3-5 and June 20-22. Sec., Dr. J. N. Baker, 517 Dexter Ave., Montgomery.

ARIZONA: *Basic Science*. Tucson, Dec. 20. Sec., Dr. Robert L. Nugent, Science Hall, University of Arizona, Tucson.

ARKANSAS: *Medical (Regular)*. Little Rock, Nov. 3-4. Sec., State Medical Board of the Arkansas Medical Society, Dr. L. J. Kosminsky, Texarkana. *Medical (Eclectic)*. Little Rock, Nov. 3. Sec., Dr. Clarence H. Young, 1415 Main St., Little Rock.

CALIFORNIA: *Reciprocity*. Los Angeles, Nov. 16. Sec., Dr. Charles B. Pinkham, 420 State Office Bldg., Sacramento.

COLORADO: *Basic Science*. Denver, Dec. 7-8. Sec., Dr. Esther B. Starks, 1459 Ogden St., Denver.

CONNECTICUT: *Medical (Regular)*. Hartford, Nov. 8-9. Sec., Dr. Thomas P. Murdock, 147 W. Main St., Meriden. *Medical (Homeopathic)*. Derby, Nov. 8-9. Sec., Dr. Joseph H. Evans, 1488 Chapel St., New Haven.

DELAWARE: Dover, July 11-13. Sec., Medical Council of Delaware, Dr. Joseph S. McDaniel, 229 S. State St., Dover.

DISTRICT OF COLUMBIA: *Basic Science*. Washington, Dec. 26-27. *Medical*. Washington, Jan. 9-10. Sec., Commission on Licensure, Dr. George C. Ruhland, 203 District Bldg., Washington.

FLORIDA: Jacksonville, Nov. 14-15. Sec., Dr. William M. Rowlett, Box 786, Tampa.

INDIANA: Indianapolis, June 20-22. Sec., Board of Medical Registration and Examination, Dr. J. W. Bowers, 301 State House, Indianapolis.

KANSAS: Topeka, Dec. 13-14. Sec., Board of Medical Registration and Examination, Dr. J. F. Hassig, 905 North 7th St., Kansas City.

KENTUCKY: Louisville, Dec. 6-8. Sec., State Board of Health, Dr. A. T. McCormack, 620 S. Third St., Louisville.

MAINE: Portland, Nov. 8-9. Sec., Board of Registration of Medicine, Dr. Adam P. Leighton, 192 State St., Portland.

MARYLAND: *Medical (Regular)*. Baltimore, Dec. 13-16. Sec., Dr. John T. O'Mara, 1215 Cathedral St., Baltimore. *Medical (Homeopathic)*. Baltimore, Dec. 13-14. Sec., Dr. John A. Evans, 612 W. 40th St., Baltimore.

MASSACHUSETTS: Boston, Nov. 8-10. Sec., Board of Registration in Medicine, Dr. Stephen Rushmore, 413-F State House, Boston.

MISSISSIPPI: *Reciprocity*. Jackson, December. Asst. Sec., State Board of Health, Dr. R. N. Whitfield, Jackson.

NEBRASKA: Lincoln, Nov. 25-26. Dir., Bureau of Examining Boards, Mrs. Clark Perkins, State House, Lincoln.

NEVADA: Carson City, Nov. 7-9. Sec., Dr. John E. Worden, Capitol Bldg., Carson City.

NEW HAMPSHIRE: Concord, March 9-10. Sec., Board of Registration in Medicine, Dr. Fred E. Clow, State House, Concord.

NEW YORK: Albany, Buffalo, New York and Syracuse, Jan. 23-26. Chief, Bureau of Professional Examinations, Mr. Herbert J. Hamilton, 315 Education Bldg., Albany.

NORTH CAROLINA: *Reciprocity*. Raleigh, December. *Examination*. Raleigh, June 19. Sec., Dr. William D. James, The Hamlet Hospital, Hamlet.

NORTH DAKOTA: Grand Forks, Jan. 3-6. Sec., Dr. G. M. Williamson, 4½ S. Third St., Grand Forks.

OHIO: Columbus, Dec. 7-9. Sec., State Medical Board, Dr. H. M. Platter, 21 W. Broad St., Columbus.

OKLAHOMA: *Basic Science*. Oklahoma City, Nov. 30. Sec. of State, Hon. Frank C. Carter, State Capitol Bldg., Oklahoma City. *Medical*. Oklahoma City, Dec. 14. Sec., Dr. James D. Osborn, Jr., Frederick.

OREGON: *Basic Science*. Portland, Nov. 19. Sec., State Board of Higher Education, Mr. Charles D. Byrne, University of Oregon, Eugene.

PENNSYLVANIA: Philadelphia, January. Sec., Board of Medical Education and Licensure, Dr. James A. Newpher, 400 Education Bldg., Harrisburg.

SOUTH CAROLINA: Columbia, Nov. 8. Sec., Dr. A. Earle Boozer, 505 Saluda Ave., Columbia.

SOUTH DAKOTA: Pierre, Jan. 17-18. Director of Medical Licensure, Dr. B. A. Dyar, State Board of Health, Pierre.

TEXAS: Houston, Nov. 14-16. Sec., Dr. T. J. Crowe, 918-20 Mercantile Bldg., Dallas.

VERMONT: Burlington, Feb. 14. Sec., Board of Medical Registration, Dr. W. Scott Nag, Underhill.

VIRGINIA: Richmond, Dec. 14-16. Sec., Dr. J. W. Preston, 30½ Franklin Road, Roanoke.

WEST VIRGINIA: Bluefield, Oct. 31-Nov. 2. Sec., Public Health Council, Dr. Arthur E. McClue, State Capitol, Charleston.

WISCONSIN: *Basic Science*. Milwaukee, Dec. 3. Sec., Prof. Robert N. Bauer, 3414 W. Wisconsin Ave., Milwaukee. *Medical*. Madison, Jan. 10-14. Sec., Dr. Henry J. Gramling, 2203 S. Layton Blvd., Milwaukee.

NATIDNAL BOARD OF MEDICAL EXAMINERS
SPECIAL BOARDS

Examinations of the National Board of Medical Examiners and *Special Boards* were published in THE JOURNAL, October 22, page 1587.

Pennsylvania July Examination

Dr. James A. Newpher, secretary, State Board of Medical Education and Licensure, reports the examination held at Philadelphia and Pittsburgh, July 5-9, 1938. Four hundred and ninety candidates were examined, 487 of whom passed and three failed. The following schools were represented:

School	PASSED	Year Grad.	Number Passed
College of Medical Evangelists	(1938)		1
Stanford University School of Medicine	(1937)		1
George Washington University School of Medicine	(1937, 8)		8
Georgetown University School of Medicine	(1936, 14)		15
Howard University College of Medicine	(1937, 3)		3

University of Georgia School of Medicine	(1933)	1
Loyola University School of Medicine	(1937), (1938, 5)	6
Rush Medical College	(1936), (1937, 3)	4
State University of Iowa College of Medicine	(1937, 2)	2
University of Kansas School of Medicine	(1928)	1
University of Louisville School of Medicine	(1937)	1
Johns Hopkins University School of Medicine	(1936), (1937)	2
University of Maryland School of Medicine and College of Physicians and Surgeons	(1937, 6)	6
Harvard University Medical School	(1936, 3), (1937, 2)	5
St. Louis University School of Medicine	(1937, 5)	5
Washington University School of Medicine	(1937, 2)	2
Columbia Univ. College of Phys. and Surgeons	(1935), (1936)	2
Cornell University Medical College	(1937)	1
New York University College of Medicine	(1937)	1
Duke University School of Medicine	(1936), (1937)	2
Eclectic Medical College, Cincinnati	(1936), (1937, 2)	3
University of Cincinnati College of Medicine	(1938)	1
Western Reserve Univ. School of Medicine	(1936), (1937, 2)	3
University of Oregon Medical School	(1936)	1
Hahnemann Medical College and Hospital of Philadelphia	(1936, 3), (1937, 69)	72
Jefferson Medical College of Philadelphia	(1935, 2), (1936, 19), (1937, 65)	86
Temple Univ. School of Med.	(1933), (1936, 11), (1937, 56)	68
Univ. of Pennsylvania School of Med.	(1936, 39), (1937, 44)	83
University of Pittsburgh School of Medicine	(1937, 60)	60
Woman's Med. College of Penna.	(1935), (1936, 2), (1937, 9)	12
Medical College of the State of South Carolina	(1936), (1937)	2
Baylor University College of Medicine	(1937)	1
University of Texas School of Medicine	(1936)	1
Medical College of Virginia	(1937, 4)	4
Dalhousie University Faculty of Medicine	(1937)	1
University of Toronto Faculty of Medicine	(1929)	1
McGill Univ. Faculty of Medicine	(1931), (1934), (1937)	3
Medizinische Fakultät der Univ. Wien	(1936, 3), (1937, 3)	6
Licentiate of the Royal College of Physicians of London and Member of the Royal College of Surgeons of England	(1927), (1936)	2
Ludwig-Maximilians-Universität Medizinische Fakultät, München	(1923), (1936), (1937)	3
Universität Rostock Medizinische Fakultät	(1924)	1
Regia Università degli Studi di Roma, Facoltà di Medicina e Chirurgia	(1936)	1
Licentiate of Royal College of Physicians and Surgeons, Glasgow	(1936)	1
University of Glasgow Medical Faculty	(1933)	1
Universität Basel Medizinische Fakultät	(1935)	1

School	FAILED	Year Grad.	Number Failed
Hahnemann Med. College and Hospital of Philadelphia	(1937)		1
University of Pennsylvania School of Medicine	(1936)		1
Regia Università degli Studi di Roma, Facoltà di Medicina e Chirurgia	(1936)		1

Forty-three physicians were licensed by reciprocity and nine physicians were licensed by endorsement from February 18 through September 12. The following schools were represented:

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
Georgetown University School of Medicine	(1934)		New Jersey
Loyola University School of Medicine	(1935)		Indiana,
New York Northwestern University Medical School	(1928)		Michigan,
(1930) Iowa			
Rush Medical College	(1936)		Illinois
University of Illinois College of Medicine	(1936)		Illinois
State University of Iowa College of Medicine	(1936)		Iowa
University of Kansas School of Medicine	(1936)		Kansas
Johns Hopkins University School of Medicine	(1936)		Maryland
University of Maryland School of Medicine	(1936)		Maryland
College of Physicians and Surgeons	(1929) Ohio, (1937)		Maryland
University of Minnesota Medical School	(1933)		Minnesota
University of Nebraska College of Medicine	(1920)		New York,
(1928) Massachusetts			
Columbia Univ. College of Physicians and Surgeons	(1932)		New York
New York Homeopathic Med. Col. and Flower Hosp.	(1925)		New York
Syracuse University College of Medicine	(1928), (1934)		New York
University of Cincinnati College of Medicine	(1934)		Ohio
Western Reserve University School of Medicine	(1934)		Ohio
Hahnemann Medical College and Hospital of Philadelphia	(1934)		Maryland,
Jefferson Medical College of Philadelphia	(1931), (1937)		New Jersey
(1934) Ohio, (1917), (1932), (1936, 2) (1937) New Jersey			N. Carolina,
Temple University School of Medicine	(1932)		California,
(1934) New Jersey, (1936) Connecticut, Utah			
University of Pennsylvania School of Medicine	(1931)		Delaware,
(1932) New Jersey, (1934) New York			
Medical College of the State of South Carolina	(1934)		S. Carolina
Medical College of Virginia	(1930)		N. Carolina
University of Virginia Department of Medicine	(1903)		New Jersey,
(1936) West Virginia			

School	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
College of Medical Evangelists	(1938)		B. M. Ex.
University of Michigan	(1937)		B. M. Ex.
Duke University School of Medicine	(1937)		B. M. Ex.
Jefferson Medical College of Philadelphia	(1932), (1934), (1937)		N. B. M. Ex.
Temple University School of Medicine	(1933)		N. B. M. Ex.
University of Pennsylvania School of Medicine	(1931)		N. B. M. Ex.
Woman's Medical College of Pennsylvania	(1935)		N. B. M. Ex.

Maryland June Examination

Dr. John T. O'Mara, secretary, Board of Medical Examiners of Maryland, reports the written examination held at Baltimore, June 21-24, 1938. The examination covered nine subjects and included ninety questions. An average of 75 per cent was required to pass. One hundred and ninety-five candidates were examined, 179 of whom passed and sixteen failed. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
University of Southern California School of Medicine....	(1938)		87
Yale University School of Medicine.....	(1936)		88
George Washington University School of Medicine.....	(1937)		82.2
83, 83.5, (1938) 81.3, 84.4, 85, 86.5, 90.3			
Georgetown University School of Medicine.....	(1938)		89.2
Howard University College of Medicine.....	(1938)		85
Loyola University School of Medicine.....	(1938)		84.5
Rush Medical College.....	(1937)		87.5
School of Medicine of the Division of Biological Sciences.....	(1937)		87.1
Johns Hopkins University School of Medicine.....	(1934)		87.6
(1935) 81.4, (1937) 78, 81.1, 85, 86, 86, 89, (1938)			
79, 79.5, 80, 80, 81, 82, 82, 82.1, 83, 83, 83, 83, 83,			
83.1, 83.2, 83.5, 84, 84, 84, 84.1, 84.2, 84.5, 85, 85,			
85, 85, 85.1, 85.1, 85.4, 86, 86, 86.2, 86.3, 86.5, 86.5,			
86.5, 87, 87, 87.1, 87.2, 87.4, 87.6, 88, 88, 88.1, 88.2,			
88.5, 88.6, 88.6, 89, 89.2, 89.3, 89.6, 90.1, 91, 91.2,			
91.3, 92.3			
University of Maryland School of Medicine and College of Physicians and Surgeons.....	(1937)		78.7
84, (1938) 78.4, 80, 80, 80, 80.3, 80.5, 81, 81, 81.2,			
82, 82, 82, 82, 82.4, 83, 83, 83.2, 83.3, 83.4, 83.4, 84,			
84, 84, 84, 84.3, 84.5, 84.6, 85, 85, 85.1, 85.4, 85.5,			
86, 86, 86.2, 86.2, 86.4, 86.4, 87, 87, 87, 87, 87.1, 87.1,			
87.2, 87.4, 87.5, 87.6, 88, 88, 88.1, 88.2, 88.2, 88.3,			
89, 89, 89, 89.1, 89.3, 89.4, 90.1, 90.3, 90.4, 90.4, 90.5,			
91, 91, 91, 91, 92, 92.3, 92.3, 94			
Tufts College Medical School.....	(1937)		85.3
University of Minnesota Medical School.....	(1938)		87.4
Cornell University Medical College.....	(1938)		82.5
Long Island College of Medicine.....	(1936)		79
University of Rochester School of Medicine.....	(1934)	80, 85	
University of Oklahoma School of Medicine.....	(1938)		84
Jefferson Medical College of Philadelphia.....	(1937)		84.1
Temple University School of Medicine.....	(1937)		85.5
University of Pennsylvania School of Medicine.....	(1937)		83
University of Virginia Department of Medicine.....	(1934)		81
University of Wisconsin Medical School.....	(1935)		81
Eberhard-Karls-Universität Medizinische Fakultät, Tübingen.....	(1936)		85.6
Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin.....	(1933)		79.5
Johann Wolfgang Goethe-Universität Medizinische Fakultät, Frankfurt-am-Main.....	(1924)		84.5
Regia Università degli Studi di Bologna. Facoltà di Medicina e Chirurgia.....	(1935)	80.5, 82.3	
Regia Università degli Studi di Roma. Facoltà di Medicina e Chirurgia.....	(1935) 77, (1936) 77.3, 77.4, 82		
Regia Università di Napoli Facoltà di Medicina e Chirurgia.....	(1936)		81
Université de Genève Faculté de Médecine.....	(1936)		79.1
School	FAILED	Year Grad.	Per Cent
George Washington University School of Medicine.....	(1937)		
Melharry Medical College.....	(1938)		
Medizinische Akademie Düsseldorf.....	(1932)		
Universität Rostock.....	(1928)		
Regia Università degli Studi di Catania. Facoltà di Medicina e Chirurgia.....	(1937, 3)		
Regia Università degli Studi di Firenze. Facoltà di Medicina e Chirurgia.....	(1936)		
Regia Università degli Studi di Messina. Facoltà di Medicina e Chirurgia.....	(1932)		
Regia Università degli Studi di Roma. Facoltà di Medicina e Chirurgia.....	(1936)		
Regia Università di Napoli Facoltà di Medicina e Chirurgia.....	(1935, 2), (1936)		
Universität Basel Medizinische Fakultät.....	(1936)		
Universität Zürich Medizinische Fakultät.....	(1937)		

Twenty-three physicians were licensed by reciprocity and eight physicians were licensed by endorsement from January 20 through July 29. The following schools were represented;

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
College of Medical.....	(1925)		California
Georgetown University.....	(1935)		Dist. Colum.
Bennett Medical College, Chicago.....	(1913)		Ohio
Chicago College of Medicine and Surgery.....	(1916)		Illinois
Northwestern University Medical School.....	(1934), (1936)		Illinois
Rush Medical College.....	(1930)		Illinois
University of Illinois College of Medicine.....	(1933)		N. Carolina
Johns Hopkins University School of Medicine.....	(1937)		N. Carolina
University of Maryland School of Medicine and College of Physicians and Surgeons.....	(1937)		Penna.
St. Louis University.....			Missouri
Washington University.....			

Temple University School of Medicine.....	(1929), (1932)	
University of Pennsylvania School of Medicine.....	(1930)	
Baylor University College of Medicine.....	(1930)	
University of Texas School of Medicine.....	(1930)	
Medical College of Virginia.....	(1936)	
University of Virginia Department of Medicine.....	(1933)	
University of Toronto Faculty of Medicine.....	(1934)	
Leopold-Franzens-Universität Medizinische Fakultät, Innsbruck.....	(1936)	New

School	LICENSED BY ENDORSEMENT	Year Endorsement Grad.
College of Medical.....		
Yale University School of Medicine.....		
Georgetown University.....		
University of Louisville.....		
Johns Hopkins University.....		
University of Oklahoma.....		
Temple University School of Medicine.....		

National Board of Medical Examiners

The National Board of Medical Examiners reports that certificate was awarded to 517 applicants who were successful in the examinations in Part III held during June and July 1938. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
University of Alabama.....	(1936)		
College of.....			
Stamford University School of Medicine.....	(1938, 3)		
University of California Medical School.....	(1937, 2), (1938)		
University of Southern California School of Medicine.....	(1938)		
Univ. of Colorado School of Med.....	(1935), (1936, 3), (1937, 4)		
Yale University School of Medicine.....	(1932), (1933, 2), (1934), (1935, 3), (1936, 10), (1937, 20)		
George Washington Univ. School of Med. (1936, 4), (1937, 6)			
Georgetown University School of Medicine.....	(1934), (1935, 4), (1936, 12), (1937, 25)		
Howard University College of Medicine.....	(1934), (1936, 2)		
Emory University School of Medicine.....	(1936, 2)		
University of Georgia School of Medicine.....	(1937, 2)		
Loyola University School of.....			
Northwestern University Medical College.....			
Rush Medical College.....			
School of Med. of the Division of Biological Sciences.....	(1937, 1)		
University of Illinois College of Medicine.....	(1936), (1937, 2)		
State Univ. of Iowa College of Medicine.....	(1937, 2)		
University of Kansas School of Medicine.....	(1936, 2), (1937, 3)		
Tulane Univ. of Louisiana School of Med. (1934), (1935, 2), (1937)			
Johns Hopkins Univ. School of Med. (1934), (1935, 2), (1937, 12)			
Boston University School of Medicine.....	(1933), (1935), (1936, 6), (1937, 12)		
Harvard University Medical School.....	(1931), (1933, 2), (1934), (1935, 5), (1936, 20), (1937, 7)		
Tufts College Medical School.....	(1933), (1935), (1936, 8), (1937, 21)		
University of Michigan Medical School.....	(1936, 2), (1937, 1)		
Wayne University College of Medicine.....	(1937)		
University of Minnesota Medical School.....	(1931)		
St. Louis University School of.....			
Washington University School of Medicine.....	(1933), (1935), (1936), (1937, 3)		
University of Nebraska College of Medicine.....	(1936, 2)		
Albany Medical College.....			
Columbia University.....			
Georgetown University.....			
Cornell Univ. Med. College (1934), (1935), (1936, 6), (1937, 5)			
Long Island College of Medicine.....	(1937, 6)		
New York Homeopathic Med. College and Flower Hosp. (1933)			
New York Med. College and Flower Hosp. (1936, 27)			
New York University, University and Bellevue Hospital Medical College.....	(1933)		
New York University College of Medicine.....	(1936, 2), (1937, 5)		
Syracuse University College of Medicine.....	(1936, 2), (1937)		
University of Buffalo School of Medicine.....	(1932), (1936)		
University of Rochester School of Medicine.....	(1937)		
Duke University School of Medicine.....	(1934), (1937)		
Western Reserve University School.....			
University of Oklahoma School of.....	(1934)		
University of Oregon Medical.....			
Hahnemann Med. College and.....			
Jefferson Medical College of.....			
Temple University School of.....			
Univ. of Pennsylvania School.....			
Woman's Medical College of.....			
Medical College of the State.....	(1937)		
Melharry Medical College.....	(1936)		
University of Tennessee College of Medicine.....	(1934), (1937, 5)		
University of Vermont College of Medicine.....	(1937, 2)		
Medical College of V.....	(1938, 5)		
Marquette University.....	(1937)		
University of Manitoba.....	(1937, 2)		
Dalhousie University Faculty of Medicine.....	(1937)		
University of Toronto Faculty of Medicine.....	(1936, 3), (1937, 4)		
McGill University Faculty of Medicine.....	(1936)		
Medizinische Fakultät der.....	(1936)		
West China Union University.....	(1935)		
Regia Università degli Studi di Perugia. Facoltà di Medicina e Chirurgia.....	(1936)		
University of Edinburgh Faculty of Medicine.....	(1936)		

Book Notices

The Culture of Organs. By Alexis Carrel and Charles A. Lindbergh. 11th. Price, \$4.50. Pp. 221, with 110 illustrations. New York: Paul Hoeber, Inc., 1938.

This book illustrates the advances that may be expected in medicine when ample research funds make possible the collaboration on a single research project of experts in many different fields. The technic of cultivation of whole organs the Lindbergh pump is described in detail, and the results of some of the cultures of whole organs are described and illustrated as proof of the efficiency of the method. The description of the construction, principle, manner of assembly, operation and operation of the apparatus are by Charles A. Lindbergh. The description of the perfusing mediums, the preparation of operating material and antiseptic solutions are borrowed from the book by R. C. Parker, *Methods of Tissue Culture* (New York, Paul C. Hoeber, Inc., 1938). The introduction and chapters on preparation of organs and anatomic regions and on behavior of organs outside the body and the conclusions are by Alexis Carrel.

The principle of the method is the forcing of a pulsating stream of sterile perfusion medium through the artery of the excised organ and out through the veins by pulsating gas pressure. The sterile fluid is filtered through platinum filters and sand and returns through an equalization chamber to the reservoir chamber of the perfusion pump, from which it is pumped again through the organ. The apparatus used is mechanically ingenious but extremely complex and, in its present state of perfection, obviously expensive to construct and practical to operate only when the collaboration of a highly skilled surgical team, mechanic, glass blower, biochemist and technician is possible. The authors give credit to fourteen killed assistants in the preface of the book. The apparatus permits control of systolic and diastolic pressures, pulsation rates and maintenance of sterility during continuous circulation of as much as 400 cc. of perfusion medium over prolonged periods. The apparatus as now constructed will permit perfusion of a 200 mg. organ for as long as a week and as a result of changing organs from one perfusion pump to another a few organs have been kept alive in part for as long as from thirty to forty days. Most of the work has been done on cat thyroid tissue, but cat ovaries and testes, the hind leg of a guinea pig fetus, and various other small organs from cats, chickens and rabbits have also been cultured, as well as small fragments of human thyroid. The illustrations consist of photographs and diagrams of the apparatus, and black and white reproductions of photomicrographs of the tissues cultured and their controls. It is well printed and bound but, unfortunately, lacks an index. It should prove indispensable to any one wishing to repeat the authors' work, of value to any one doing tissue cultures, and of great interest to physicians and scientists who are interested in the fundamental problems of the nature and functions of living tissue.

The meticulous attention to detail evidenced throughout the book illustrates again the truth in the adage that "genius means an infinite capacity for taking pains."

Die "postvaccinale Encephalitis" nach amtlichen österreichischen Daten. Von Dr. Marius Kaiser, Ministerialrat im Bundesministerium für soziale Verwaltung, und Hofrat Dr. Julius Zappert, Universitätsprofessor in Wien. Paper. Price, 4.80 marks. Pp. 97. Vienna: Julius Springer, 1938.

This monograph is crowded with interesting epidemiologic and clinical observations. In 1801 and 1802 the official reports for Bohemia listed in a series of 10,090 vaccinations thirty-five cases of a central nervous system disease which today would be diagnosed as postvaccinal encephalitis. Between 1925 and 1935 240 cases of this complication with a mortality of seventy-three (30.4 per cent) were diagnosed in Austria. Although the malady had reached a low level in England and the Netherlands, forty cases were seen in 1933. It is noteworthy that the susceptibility for this complication is low during the first five years of life despite the large number of vaccinations. It reached its highest incidence in the age groups 7 to 9. A greater liability of the females is shown in the relationship of 113 males to 127 females. A seasonal predominance during May to July with a

peculiar regional frequency for example in the Tyrol suggests a "locality factor" which may or may not be related to other postinfectious or primary forms of encephalitis. The authors could find no connection between the degree of the vaccinal reaction and the development of the complication. In fact, they believe that the disposition of the vaccinated and not the quality of the vaccine lymph is of importance. Neurotropic properties were not demonstrable in the Austrian vaccinia. The "incubation time"—the period which elapsed between the vaccination and the symptoms of encephalitis—averaged 10.8 days. Predominantly an encephalitic process proved clinically and by forty-five carefully conducted necropsies, meningitic, myelitic and even bulbar types have been observed. Causal treatment with convalescent serum has been tried but no definite data are recorded. Under prophylaxis, the primary vaccination during the first year of life receives special emphasis.

A History of Dentistry. By Arthur Ward Lufkin, D.D.S., Assistant Professor of Dental History in the College of Dentistry, University of Southern California, Los Angeles. Cloth. Price, \$2.75. Pp. 255, with 90 illustrations. Philadelphia: Lea & Febiger, 1938.

The best chapter of this history is the first one, on the antiquity of dental disease, included in the section devoted to the first era, which covers the period up to the time of the Arabian invasion of Europe. Scant sixteen pages are devoted to the second era, entitled the Dark Ages. This is unfortunate, as herein is laid the foundation for the modern period, or third era. The material for this last period is assembled in three chief portions, entitled France, Great Britain and the United States. In these chapters too much attention is paid to legislation and education. The text is arranged for the most part in the form of short encyclopedic paragraphs and without much continuity of thought. The point of view of the last chapter, on the crystallization of a new concept of dentistry, is narrow and should either be eliminated or greatly modified. The author assumes that his readers will have a background inadequate to orient dental history with world history and therefore from time to time inserts material of a general character. The compilation of facts, data and bibliographic material apparently has been done with great care, as no noteworthy errors have been detected. It would seem that the author has missed a real opportunity to supply a greatly needed, condensed but adequate history of dentistry for use in schools and by persons interested in dentistry and its background.

Traité de pharmacie chimique. Par P. Lebeau, professeur à la Faculté de pharmacie de Paris, et G. Courtois, assistant à la Faculté de pharmacie de Paris. Tome I: Chimie minérale et chimie organique (Série acyclique). Tome II: Chimie organique. Fascicule I: Séries cyclique et terpénique, dérivés azotés acycliques et cycliques, vitamines et hormones, composés organo-minéraux; série hétérocyclique, matières colorantes, alcaloïdes, glycosides et albuminoïdes. Fascicule II: Série hétérocyclique, matières colorantes, alcaloïdes, glycosides et albuminoïdes. Second édition. Cloth. Price, Tome I, 250 francs; Tome II (2 fascicules), 460 francs. Pp. 1,206; 1,063; 1,061. Paris: Masson & Cie, 1938.

In spite of the size of this work the authors say it remains both a text and a reference book; that the student may find in the heads of chapters and in the principal articles all that corresponds to the program of instruction in chemical pharmacy given by the Faculty of Pharmacy in Paris.

The object of chemical pharmacy is the study of chemical elements and compounds used in therapeutics. The student should have adequate knowledge concerning their manufacture, origin of primary materials, process of preparation and national production. To show the rapid growth of chemical pharmacy they point out that the French Codex in 1837 contained 187 medical chemicals (galenicals excluded) while in 1937 it contains 355 and the extrapharmacopoeial products in use number more than 2,000.

Volume I deals with inorganic, and the acyclic series of organic, chemistry. Commencing with hydrofluoric acid, which is described rather fully, the authors list sixteen fluorides and give their solubilities and the p_n of their saturated solutions. For the usages of sodium fluoride they say "It is used for the lavage of wounds, as a surgical antiseptic, for lavage of the bladder (1 in 500) and in obstetrics (1 in 600)." In discussing tin they say "Tin in the form of a powder is indicated as a vermifuge in dose of 10 to 15 grains." The pharmacology,

which is a secondary object, is definitely a weakness of the work. Under mercury, the addition of the metal itself, sixteen inorganic combinations and more than twenty of its organic compounds are described, and perhaps as many more organic compounds under the corresponding anions. This explains why the work is voluminous without the subjects being treated extensively. The acyclic series is rather fully described in the order usual in chemical textbooks. The whole volume has been carefully read and a list of errors (which are few) is given with corrections.

Volume II is divided into two parts: Part I deals with medicaments furnished by the cyclic series and terpenes, nitrogen derivatives acyclic and cyclic, and organic combinations with minerals. Vitamins and hormones are included in this part. As an indication of the inclusiveness of this work, they discuss the following salicylates: Na, Li, Mg, Zn, Cd, Al (basic), Hg (basic), Bi (basic), Ti (basic). The therapeutic uses of these are given. In addition to these they say that some therapeutic uses of the following have been established, for which they give the chemical formulas and solubility in water: K, NH₄, Ca, Ba, Fe, Ur, Pb and Cu. Part 2 includes medicaments furnished by the heterocyclic series, coloring matters, alkaloids, glucosides and albuminoids.

From the medical point of view it is deplorable that chemists and pharmacists feel they must include so many drugs of questionable value and that are quite unnecessary. Yet the practicing physicians are to blame. If physicians paid more attention and limited themselves to official or accepted drugs, pharmacy would be less onerous and quite as valuable. One gets the definite impression from this work that French chemistry and pharmacy are far superior to French pharmacology. Chemists and pharmacists accept statements of therapeutic uses that pharmacologists would reject as based on insufficient evidence. Again the inclusion of such therapeutic uses in a book on chemical pharmacy by prominent authors is accepted by many physicians and acts as a vicious circle to perpetuate the use of many drugs of little or no value.

As a reference book in medical chemistry, this work is reliable and has considerable value; but for American workers it is not indispensable. The references are numerous but not complete; the authors state frankly that this is a task almost impossible to realize. As a textbook it seems too voluminous for chemical pharmacy alone, yet it contains much extratropical matter that is decidedly valuable for general information and education. The student who masters its contents in a passable degree must have a wide knowledge of chemical pharmacy.

Fundamentals of Biochemistry with Laboratory Experiments. By Carl L. A. Schmidt, M.S., Ph.D., Professor of Biochemistry, University of California, and Frank Worthington Allen, Ph.D., Instructor in Biochemistry, University of California. Cloth. Price, \$3. Pp. 388, with 29 illustrations. New York & London: McGraw-Hill Book Company, Inc., 1938.

As indicated in the title, this is a combination of textbook and laboratory manual. Naturally, considerable abbreviation is necessary to cover the subject matter in a book of this size. This is rather unfortunate, because the treatment of the discussions and laboratory instructions are frequently so condensed that the student no doubt is either forced to consult other textbooks or to repeat experiments in order to obtain correct results. The order of presentation appears irregular in part; thus, neutrality regulations in the body, enzymes, mineral metabolism, vitamins and the chemistry and functions of the endocrine secretions are discussed before the chemistry of the lipids, carbohydrates and proteins is considered. The chemistry of these cell constituents is discussed briefly and in an elementary manner and the laboratory treatment is equally condensed. Although the discussions on hydrogen ion concentration and neutrality regulation in the body are well presented, the experimental procedures for the measurement of hydrogen ion concentration and of alkali reserve in plasma are not adequately described. The modern manometric methods are not referred to. In the discussion on the effect of traces of carbonate in the titration of standard sodium hydroxide by standard hydrochloric acid it is stated that the pink color assumed by the phenolphthalein when the colorless solution is heated is produced by the carbonate ion. Why not say it is due to the hydrolytic dissociation of the sodium

carbonate into sodium, bicarbonate and hydroxyl ions? It is difficult to explain why so unimportant a reagent as Barium solution is described and used but no mention made of Fehling solution, furfural reactions, imidazole reactions, ninhydrin, various amino acid reactions and the detection of phenols and hemoglobin. On the other hand the laboratory instructions emphasize more than usual the physiologic type of experiments, many of which are good but which can be satisfactory only when not conducted and of necessity therefore time consuming. The book closes with a valuable chapter on dietary data and illustrates problems in biochemistry.

An Introduction to Dermatology, with a Chapter on the Theory and Technique of X-Ray and Radium Therapy. By E. H. Molesworth, M.B. Ch.B., Lecturer in Diseases of the Skin, University of Sydney. Foreword by Professor Josef Jadassohn. Cloth. Price, 25s. Pp. 320, with 117 illustrations. London: J. & A. Churchill, Ltd., 1937.

Molesworth's textbook opens with a foreword by the late Prof. Josef Jadassohn, and the influence of his teachings is noted in the text. The discussion on allergic diseases embraces eczema, occupational diseases, urticaria and purpura. There is also a discussion of sensitization and desensitization with remarks on cutaneous testing, including patch testing. This entire section occupies fifty-seven pages. For some unexplained reason the author includes urticaria pigmentosa under the general heading of allergic diseases. The remarks on the treatment of the various described dermatoses are conservative and practical. The book is well illustrated, but the photographic reproductions, on the whole, do not compare in excellence with those in our better American textbooks. The section on radiation treatment is excellent and contains the fruit of the author's wide experience in the treatment of carcinoma of the skin, a condition occurring with great frequency in Australia. The author has attempted with considerable success to explain the simple physical problems of radiation treatment. This discussion is particularly recommended to dermatologists or to those who have occasion to treat superficial epitheliomas with x-rays. On page 389 there is confusion in the titles Schamberg's disease and Majocchi's disease. In this country progressive pigmentary dermatosis is considered to be Schamberg's disease and purpura annularis telangiectodes Majocchi's disease.

Control Narcotics Intelligence Bureau, Egyptian Government, Annual Report for the Year 1937. Paper. Price, P. T. 10. Pp. 204, with 114 illustrations. Bulâq, Cairo: Govt. Press, 1938.

The first four chapters of this report deal with the results of the application of new narcotic laws in the apprehension and punishment of traffickers in opiates and hashish in Egypt. Many case reports are given showing the quantity of the drugs confiscated, the names and the nationalities of the offenders apprehended, and the sentences inflicted. Methods used by both traffickers in drugs and the agents who set about to apprehend them are given in some detail and do not differ materially from the methods used in other parts of the world. New legislation in Egypt provides severe punishment for the violation of the narcotic laws not only for natives but also for foreigners. This is something new in Egypt and has been a boon to the narcotic agents. There is also new legislation directed at drastic reduction in the cultivation of both hashish and opium poppies within Egypt.

It appears that Egypt's problem will be a difficult one because of the fact that most of the movement of illicit heroin from its sources to its several destinations must be through the Suez Canal, and the danger of smuggling portions of this drug into Egypt while en route constitutes a real source of danger to the country. There follow reports on the progress of several countries in the treatment of addiction and the reduction of international traffic in opium and hashish.

The next portion of the report is given over to tables delineating narcotics seized by coast guards, customs and police authorities on port steamers from Jan. 12, 1936, to Jan. 11, 1937, and tables showing a progressive reduction in seizures of hashish, manzoul, cocaine and heroin from 1929 through 1937, with a concomitant rise in the seizure of opium in the last year or so. Where it is possible to determine the source or origin of drugs seized, this information is noted in tables listing the name of the offender, the quantity and the nature

the drug, and the source. It appears that India is the chief source of hashish, followed by Syria, and that China furnishes most of the opium. The bulk of the heroin seized could not be traced to its source.

A study of the incidence of addiction revealed greater numbers near the Suez Canal and the Palestine frontier. Hashish is the drug of choice, followed by opium and heroin. Abundant tabular data give information on addicts and traffickers, their characteristics, convictions, social effects, methods, addiction and profits.

Nutritional Physiology of the Adult Ruminant. By Ernest G. Ritzman, Research Professor in Animal Nutrition, New Hampshire Agricultural Experiment Station, and Francis G. Benedict, Director, Nutrition Laboratory, Carnegie Institution of Washington. Carnegie Institution of Washington Publication No. 494. Paper. Pp. 200, with 5 illustrations. Washington, D. C., 1938.

This volume presents portions of the results of fifteen years of cooperative research by the New Hampshire Agricultural Experiment Station and the Nutrition Laboratory of the Carnegie Institution. A large number of observations are summarized and discussed, providing a useful digest of current knowledge. Numbers of cows, steers, bulls, goats, sheep and swines were studied particularly from the point of view of energy exchange and diet utilization. The results are of practical as well as theoretical importance. One is impressed by the fragmentary knowledge of the physiology of domestic animals of economic importance, as compared with the more complete knowledge of dogs, cats, rabbits and rodents, which are more usual laboratory animals. The need for more intensive study of the farm animals is made apparent. Fragmentary data on urine, feces, heart rate, respiratory rate and body temperature are given.

Standards for the Diagnosis and Treatment of Cancer. By the Executive Cancer Committee of the Iowa State Medical Society. Paper. Pp. 12. Iowa City, Iowa: Athens Press, [n. d.].

Admittedly for the purpose of reference on the part of the general practitioner, the cancer manual developed by the Executive Cancer Committee of the Iowa State Medical Society is practical, clear and concise. After a brief introduction in which the cooperation of medical and lay educational campaigns against cancer is urged, the authors take up briefly some general considerations. In this section, as throughout the manual, the language used is simple and avoids, so far as possible, complicated terminology. This is, of course, a valuable characteristic of the book from the point of view of the general practitioner. In cancer therapy as in most other branches of medicine there is a tendency to develop specialists. Valuable as the services of these highly trained men may be, there is also need of enlisting the support of the members of the profession who cannot restrict their practice to the field of malignant growths. To the latter group the manual should be of great assistance, for it presents for each location and type of cancer the early and late signs, the diagnosis and differential diagnosis, the treatment and the prognosis. There are two brief appendices. The first deals with grades of malignancy as described in the clinic and pathologic laboratory. The second is a discussion of radiation therapy, a valuable section for those who desire to understand the simple major premises of this type of treatment. It would be splendid for cancer control for a copy of the Iowa manual to be in the hands of every new alumnus of our medical schools on graduation and on the desk of every general practitioner in the country.

Les éléments du pronostic dans les maladies aiguës: Notes de pratique. Par A.-B. Marfan, professeur honoraire à la Faculté de médecine de Paris. Paper. Price, 20 francs. Pp. 77. Paris: Masson & Cie, 1938.

This short treatise deals with practical clinical aids useful for prognosis in the acute febrile illnesses. Typhoid, the pneumonias, diphtheria, scarlet fever, endocarditis, pericarditis and meningitis are the diseases discussed. The book has little that is new. Such signs as pulse rate and character, the appearance of the tongue, presence or absence of abdominal distention, and the quantity of urine are the features stressed in discussion of pneumonia and typhoid. Many of the prognostic signs mentioned are of little value now, owing to new modes of therapy which have altered the course of these diseases, as serum therapy in pneumonia or sulfanilamide in meningitis.

Diagnostisch-therapeutische Technik für den Chirurgen. Von Dr. med. Rudolf Gelsendörfer, I. Assistent der Chirurgischen Universitäts-Klinik Breslau. Mit einem Geleitwort von Professor Dr. K. H. Bauer. Paper. Price, 16 marks. Pp. 509, with 150 illustrations. Leipzig: Johann Ambrosius Barth, 1937.

This is a new book and is written for the use of surgical residents and interns in the surgical services in hospitals. It is a practical work, intended for daily use, and presents an abundance of useful information in compact form, in a volume of such size that it can easily be carried in the pocket. The material covered includes information on diagnosis, indications for surgical treatment, and preoperative and postoperative management of the various surgical conditions. The diagnostic information includes and particularly presents the laboratory data on the urine and the blood, the x-ray appearances and the special diagnostic tests. The book is extremely practical and the material is strictly down to date, as is evidenced by the bibliography also, most of the references being to papers published since 1930. The author has succeeded in his goal, which was to present a work suitable as a textbook for the younger assistants, a welcome reference work for older surgeons, and a pocket sized book of reference for interns.

Medical Relief in Michigan—A Study of the Experience in Ten Counties. By Nathan Sinal, Marguerite F. Hall, V. M. Hogue, and Miriam Steep. Paper. Pp. 146. Ann Arbor, Michigan: Edwards Brothers, Inc., 1938.

A detailed study of ten Michigan counties, based on a month by month analysis of all reports and statements, presents a valuable summary of many features of medical relief in Michigan. While the divergence of conditions and methods of administration made it difficult to give results applicable to all the counties, the tabulations of costs, services and all other features should be helpful to any one seeking to develop plans for medical care for the indigent. The divergences were so wide that in several instances two counties were excluded, and many of the conclusions are based on eight counties only. For these eight counties the total calls per illness averaged 1.9. "The median cost per person on relief in the eight counties during 1934" was \$11.44. However, it is recognized that the records so tabulated did not actually include all costs, and therefore it is concluded that "if the total cost of medical relief, including all hospital care, is charged against the population on general relief, as a suggested method of estimating future costs," the results would be the following table:

Medical care (homes and offices).....	\$ 3.01
Medical care (hospitals).....	3.88
Hospital	6.40
Dental care.....	.36
Nursing care.....	.50
Eye care15
Drugs	1.07
Surgical appliances, etc.....	.11
Transportation06
Administration (10 per cent).....	1.55
Total	\$17.09

Step by Step in Sex Education. By Edith Hale Swift, M.D. Cloth. Price, \$2. Pp. 207. New York: Macmillan Company, 1938.

This is not just another book attempting to gain the attention of the doctor and the parent. It is an excellent work that will serve both parent and physician. The physician who wishes to have constantly at his elbow a valuable aid to give to the perplexed parent will find this volume ideally suited for that purpose. The parent who wishes to improve his technique in answering the ever-present questions of the child will find the answers to almost all the questions any child has ever asked. The book is divided into three parts: the first deals with sex in childhood, the second with puberty and its manifestations; the third presents the sexual aspects of adolescence through and into the preparation for marriage. The author presents excellent arguments for early sex education. That sex education should be continuous is well brought out in the various steps. Not all children will ask the questions that the mythical Bert and Jane in this book have asked, but the parent will find practically all the questions that children ask ingeniously and excellently, yet easily, explained. It is not a book to give to the child but rather a text for father and mother. The adolescent will enjoy reading the book for himself.

Die offene Lungentuberkulose bei Kindern und Jugendlichen: Ein Beitrag zur Frage Tuberkulose und Konstitution. Von Professor Dr. Kurt Klare, Direktor der Tuberkulose-Kinderklinik Prinzregent-Luitpold-Schelling-Allee, und Dr. Frieda Böhmig. Paper. Price, 13.50 marks. Pp. 164, with 91 illustrations. Leipzig: Georg Thieme, 1938.

In this work the illustrations are mostly made from roentgenograms of chests. The authors have made an extensive study of tuberculosis among children and young adults. They call attention to the dangers of exposure to persons with open tuberculosis with reference to the development of first infections. They report eighty-five deaths from tuberculosis in the entire group under their observation. Only four of these deaths occurred among children under the age of 12 years and only two under the age of 11 years. Thus, their experience with reference to mortality beginning with the development of adolescence and thereafter is very similar to that reported in this country. Much emphasis is placed on other factors than the tubercle bacillus with reference to the development of clinical disease in young adults, for example, such factors as constitution and color of hair. Although many will disagree with the author's conclusions in this respect, the work is well worth reading since it contains a large amount of valuable data.

Syphilis, Gonorrhea and the Public Health. By Nels A. Nelson, B.S., M.D., F.A.P.H.A., Director, Division of Genito-Infectious Diseases, The Massachusetts Department of Public Health, and Gladys L. Crain, R.N., Epidemiologist, Division of Genito-Infectious Diseases, The Massachusetts Department of Public Health. Cloth. Price, \$3. Pp. 359, with 9 illustrations. New York: Macmillan Company, 1938.

In the foreword the authors call attention to the fact that they have written this book for public health nurses, social workers and physicians. This idea has been carried out well in that the book contains much more technical information than the recent books on syphilis for the general lay reader. For this reason the volume is recommended highly not only to public health officials, both professional and lay, and to social service workers, but as a textbook for nurses and those who have more than a passing interest in the genito-infectious diseases, a term which the authors recommend. The technical features of the book are readily understandable and are couched in terms which are intelligible to the nonprofessional group. The authors give due credit for the source of the material and acknowledge the work of the Cooperative Clinical Group as a basis for the modern treatment of syphilis. The book is highly recommended as an authentic guide to those interested in the problem of syphilis and gonorrhea, both lay and professional workers, and it is of particular value to the lay group who work with patients having these diseases. The patient who is receiving treatment for syphilis would also find much of value in the book.

Diseases of the Skin for Practitioners and Students. By George Clinton Andrews, A.B., M.D., Associate Professor of Dermatology, College of Physicians and Surgeons, Columbia University, New York. Second edition. Cloth. Price, \$10. Pp. 899, with 938 illustrations. Philadelphia & London: W. B. Saunders Company, 1938.

This is an excellent readable treatise on dermatology with numerous superb illustrations. There is a chapter on dermatoses due to vitamin deficiency, and the chapter on roentgen rays is excellently done and contains a wealth of practical and technical information. This chapter together with the one on radium and radon should be read by all dermatologists and by those who may use these agents in dermatologic therapy. The discussions on treatment are replete with prescriptions to aid the general practitioner in his attempt to treat cutaneous diseases.

Die Missbildungen und Anomalien der Nase und des Nasenrachenraumes. Von Dr. Walther Stupka, Privatdozent für Oto-Rhino-Laryngologie an der Universität in Innsbruck. Paper. Price, 36 marks. Pp. 319, with 133 illustrations. Vienna: Julius Springer, 1938.

There have been few books in recent years on congenital deformities, particularly in the field of laryngology. Stupka's work is therefore most timely. The author has made a thorough study of his subject and has painstakingly combed the literature for every bit of evidence that might help to bring it to the minute. The book is divided into the following sections: I. The origin of malformations in general, which embraces studies of developmental errors from various causes,

differential diagnosis between hereditary and malformation not due to germinal factors, determination of the time factor the origin of the malformation and the results of experimental teratology. II. Experiments on the embryo directed particularly toward influencing the development of the nasal apparatus. III. The malformations and anomalies of the nose. IV. The malformations and anomalies of the nasopharynx. Despite the complexity of the subject and the vast amount of material presented, the book is not difficult to read. To the research worker and the anatomist it should prove of inestimable value for reference. To the laryngologist who still retains some interest in embryology the book should provide interesting and valuable reading, for nowhere else can he find as complete a story of the rarer anomalies which are occasionally encountered as in this work. The illustrations are helpful and the bibliography a veritable mine of information.

Psychiatrie: Médicale, physiologique et expérimentale; Sémiologie—thérapeutique. Par H. Baruk, Médecin en chef de la Maison nationale de Charenton. Paper. Price, 220 francs. Pp. 827, with 125 illustrations. Paris: Masson & Cie, 1938.

This is not a textbook of psychiatry but a long personal report of the author's researches, his interpretations of the psychoses and his methods of treatment and, finally, remarks on the organization of psychopathic hospitals, particularly the National Hospital at Charenton, France, of which he is the physician in chief. Baruk has done extensive work on catatonia, psychoses with brain tumors and experimental convulsions. These and other papers appear in the first part of this volume. Then follow clinical cases from his wards, with methods of study and treatment. In the latter part of the book historical material is introduced, particularly on Royer-Collard, Bayle, Esquirol and other French psychiatrists who have worked at Charenton. Finally, the author gives some details regarding hospital administration. The book is well written and illustrated. The volume should be read by all physicians caring for patients with mental disorders. The account of Charenton will be appreciated by medical historians.

Agostino Bassi in the History of Medical Thought—A. Bassi and L. Pasteur—The Contagium Vivum Theory Throughout the Centuries: Aspects and Considerations. By Giovanni P. Arcieri, M.D. Paper read before the Medical Staff of the Parkway Hospital in New York at its meeting of February 23, 1938. Preface by Prof. Cesare Frugoni. Paper. Pp. 30, with portraits. New York City: Vigo Press, 1938.

The main purpose of this brief historical sketch is to forward the thesis that Spallanzani, Acerbi, Valli and especially Bassi were more important founders of the science of microbiology than were Pasteur or Koch. While some facts concerning their contributions, especially those of Bassi, are certainly not appreciated, the tendency to belittle the contributions of Pasteur, Koch and others is to be deplored and not in keeping with the true scientific spirit. The author has, nevertheless, contributed some interesting facts of historical importance to the subject.

A Synopsis of the Diagnosis of the Acute Surgical Diseases of the Abdomen. By John A. Hardy, B.Sc., M.D., F.A.C.S. Cloth. Price, \$1.50. Pp. 345, with 92 illustrations. St. Louis: C. V. Mosby Company, 1938.

This is a small pocket sized textbook which deals empirically only with the diagnosis of the acute surgical conditions of the abdomen. It is written in clear, simple, concise style with the purpose of providing "quick, accurate, and complete means for the study of these urgent diseases." Beginning with chapters on surface localization of the abdominal organs, technique and importance of physical examination and hints for obtaining a detailed history, the ensuing thirty-eight chapters discuss the diagnosis and differential diagnosis of all possible abdominal emergencies briefly but completely. In addition, a few conditions the symptoms of which may cause diagnostic confusion, such as chronic cholecystitis, duodenal ileus, hemolytic jaundice and ureteral stricture, are included. Although all possible laboratory aids to diagnosis are discussed, special emphasis is placed on the importance of the history and physical observations in establishing the diagnosis. This book, written chiefly for the general practitioner who comes in contact with the greater portion of abdominal surgery, adequately fulfils its purpose.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Libel: Attributing Authorship of Medical Article to Physician Not the Author.—The defendant, the Ethical Publishing Company, published in its periodical, *American Medicine*, an article entitled "Therapeutic Uses of Colloidal Sulphur." It attributed the authorship of the article to the plaintiff, a physician, when in fact he neither wrote it nor had anything to do with its preparation or publication. The plaintiff brought suit for libel in the city court of New York, New York County, against the defendant company. The actual author of the article, a physician, was joined as defendant. At the trial, the defendant physician admitted he had prepared the article and had read the galley proofs before publication and that the plaintiff had refused to write an article on colloidal sulfur, because the plaintiff thought the time not yet ripe for a definite statement on its uses. The plaintiff claimed the article had held him up to ridicule and contempt among his friends and professional acquaintances.

The illegal and unauthorized use of the plaintiff's name in the published article, said the court, made the article libelous per se. The plaintiff considered the publication of the article contrary to professional ethics and he had refused to have his name associated with such advertising of colloidal sulfur. The advertising features of the article, in the judgment of the court, held the plaintiff up to severe criticism in his profession. He was an impressive witness in court and appeared to be sincere in the practice of his profession and imbued with the proper respect for medical ethics. The court concluded that the nature of the libel, the social and professional position of the plaintiff and the tendency of the article to injure him in public esteem entitled him to compensatory damages, which the court fixed at \$250. Judgment for \$250 was directed against the defendant Ethical Publishing Company, which was given judgment in the same amount over against the defendant physician who wrote the article.—*Gershwin v. Ethical Pub. Co., Inc., et al. (N. Y.), 1 N. Y. S. (2d) 904.*

Workmen's Compensation Acts: Trauma in Relation to Tuberculosis of Knee Joint and Lungs.—Nyberg was employed by the defendant corporation. He was 53 years old and had led an active life. The published record does not show affirmative evidence of any illness prior to the accident under which this case arose but does show affirmatively that he had no disorder of his left knee until after the accident. On Nov. 16, 1926, Nyberg, in the course of his employment in one of the defendant's quarries, was in a squatting position, holding with both hands the handle of a "bull set," a tool used in cutting and trimming stones. This tool, as was customary when it was in use, was being struck repeatedly with a sledge-hammer by a fellow workman. One of the blows jarred the handle of the tool and jerked Nyberg's left elbow, which was resting on his left leg near the knee, and a stinging sensation in the knee followed. Nyberg rubbed the knee for a few moments and then resumed work. During the next few days he suffered from pain and numbness in the knee. The pain became progressively worse, and four or five days after the accident the knee became swollen and discolored.

Nyberg consulted a physician, who diagnosed his condition as "water on the knee" and proposed an operation. After treatment by hot water applications and iodine had failed, an operation was performed Dec. 16, 1926. The condition of the knee was then diagnosed as "an acute stage of traumatic bursitis." The operation did not produce much improvement. In 1928 a physician diagnosed Nyberg's trouble as "a low-grade inflammatory reaction" and another diagnosed it as "a low-grade infectious arthritis." Between March 1927 and March 1930 Nyberg worked for short periods for the defendant and other granite companies but after the latter date was unable to work. Early in 1933, somewhat more than six years after the accident, roentgenograms disclosed "a definite destruction of the knee joint and cartilage" and "a cold abscess, in the popliteal space."

In April 1933 tubercle bacilli were found in the sputum. Roentgenograms made shortly thereafter showed an advanced stage of pulmonary tuberculosis and tuberculosis of the left knee joint. In August 1933 Nyberg's left leg was amputated above the knee joint. Thereafter he remained in a tuberculosis sanatorium until his death in March 1935.

For seven weeks after Nyberg was injured his employer paid him compensation and paid his medical and hospital expenses. When he refused to pay further compensation and medical expenses, Nyberg instituted proceedings under the Minnesota workmen's compensation act against the employer and its insurance carrier. After his death his widow was substituted as claimant. From an award by the industrial commission granting her compensation and dependency benefits, the employer and its insurer appealed to the Supreme Court of Minnesota.

Eleven medical experts had testified in the proceedings before the case came to the Supreme Court. Both sides agreed that tuberculosis of a joint is an infection secondary to tuberculosis of the lungs. Evidence proving the presence of a dormant tuberculous infection of the knee at the time of an injury therefore proves, the Supreme Court reasoned, that the injured person had a tuberculous infection of the lungs at some earlier time. In the present case, said the court, there was considerable evidence to show that the tuberculous infection of the lungs had been arrested and was dormant when the accident to the knee occurred and that the infection of the lungs was lighted up or activated by the activation of the tuberculous infection in the knee that resulted from the accident. Such activation of the infection of the lungs may have resulted, according to several of the medical witnesses, either from a lowering of Nyberg's resistance or from a release of bacilli and toxins into his blood stream, by the actively diseased knee joint. All experts agreed that a dormant tuberculous infection might be present in the knee and be aroused into activity by a slight trauma. But while the medical experts for the claimant were of the opinion that there was a dormant tuberculous infection in Nyberg's knee when the accident occurred, which was activated by the accident, the medical experts testifying on behalf of Nyberg's employer believed that the tuberculous condition in the knee was merely a coincidence and had no causal relation to the injury.

The fact that the tuberculosis of the knee was not recognized for several years after the accident might seem to prejudice the case of the claimant. From the time of the injury until the time when tuberculosis was first diagnosed several years later, however, there was an undisputed history of a serious condition of the knee, which became progressively worse; an unbroken sequence of symptoms manifested themselves throughout this period. This gave strong support to the conclusion that the tuberculous infection became active at the time of the injury or shortly thereafter and had a direct connection with it. The rapidity of the development of tuberculosis and of the appearance of clinical symptoms after a traumatic activation of a latent tuberculous condition, said the Supreme Court, varies with the individual injured and depends to a large extent on his general resistance and on the virulence of the infecting germs. The development in some cases is prompt and rapid, in others it extends through a period of months or years. The evidence, said the court, leads to the inference that the tuberculous infection in Nyberg's knee became active about the time he was injured.

The evidence in the case justified the conclusion, said the Supreme Court, that Nyberg's tuberculous knee joint aroused into action the germs of tuberculosis that lay dormant in Nyberg's lungs and thus caused his death. A finding of a causal relation between the tuberculous knee joint and the injury sustained by Nyberg in the course of his employment was justified by competent evidence. Responsibility for his illness and death therefore rested on his employer under the workmen's compensation act.

On behalf of the employer, however, it was contended that the claim of Nyberg's widow was barred by the statute of limitations. The commencement of proceedings by an employee, however, said the Supreme Court, is notice that a claim is being made and, if it is valid, that a claim will also exist in favor of the defendants if death results from the injury. Notice that the accident is claimed to be of compensable nature, which the employer receives within the required time, is all the protection

which the six year limitation provisions of the Minnesota statute intend to give and to which the employer is entitled. Proceedings by the dependent survivor after an employee's death are not new, separate and distinct proceedings but are merely a reopening or continuation of the proceedings commenced by the employee.

The Supreme Court affirmed the award of the workmen's compensation commission in favor of the claimant.—*Nyberg v. Little Falls Black Granite Co. et al.* (Minn.), 277 N. W. 536.

Harrison Narcotic Act: Error in Physician's Narcotic Record not per se a Crime.—Section 1044(a) of the Harrison Narcotic Act, U. S. C. A., title 26, chapter 12, declares it to be unlawful for any one to sell, barter, exchange or give away any narcotic drug except in pursuance of a written order. Section 1044(c) of that act, however, authorizes the dispensing or distribution of narcotic drugs, without written orders, to patients, by a physician registered under the act, in the course of his professional practice, provided he keeps a record of all drugs within the coverage of the act that he dispenses or distributes, except such "as may be dispensed or distributed to a patient upon whom such physician, . . . shall personally attend." Furthermore, U. S. C. A., title 26, chapter 25, section 1693(a) (A) makes it unlawful to simulate or falsely or fraudulently execute or sign any entry or other document required by the internal revenue laws or by any regulation made in pursuance thereof. The defendant, a practicing physician, was convicted in the United States district court for the district of Colorado of violating both of the sections named, under a charge that he unlawfully sold, dispensed and distributed morphine to persons unknown, not in pursuance of written orders, and unlawfully, falsely and fraudulently simulated, executed and signed a narcotic record showing the amount of narcotic drugs dispensed and distributed and the names and addresses of patients to whom such drugs had been distributed. From this conviction, the defendant appealed to the United States circuit court of appeals, tenth circuit.

The conviction of the defendant physician was based on the following evidence. On Jan. 13, 1936, a federal narcotic agent seized the defendant's narcotic records and held them until the trial. Those records indicated that on Jan. 8, 1936, the defendant dispensed to "G. Hagen" twelve capsules and four ounces of a cough mixture. The capsules contained among other things one-half grain of morphine sulfate, apparently in each capsule. The cough mixture contained one grain of morphine sulfate, a half drachm of paregoric and an ounce of syrup of white pine, but whether in the ounce or in four ounces the published record does not show. According to the testimony of a Mrs. Frances Hagen, to whom the entry "G. Hagen" apparently referred, no narcotic drugs were dispensed to her on the date stated. It was shown, however, that Mrs. Hagen and a Mrs. Whalen, who was suffering from influenza, arrived at the defendant's office about the same time, that he excused himself from Mrs. Whalen's presence in order to receive a payment from Mrs. Hagen on her account, that after Mrs. Hagen's departure he dispensed to Mrs. Whalen twelve capsules containing morphine and four ounces of cough medicine such as are described above and that he entered them in his records under the name of Mrs. Hagen. There were certain discrepancies, too, in the records of the defendant's treatment of a Mrs. Smith after surgically removing a sliver from her hip. Mrs. Smith testified that the defendant gave her a narcotic drug on her second visit on January 3 and again on January 4. The defendant, however, testified that he dispensed a narcotic drug to Mrs. Smith to relieve pain on her first visit, January 1, and again January 4. Their testimony differed also as to the form in which the narcotic drugs were dispensed and the number of doses dispensed. The defendant's testimony, however, was corroborated by his narcotic record.

The defendant's dispensing of narcotic drugs to Mrs. Smith, said the circuit court of appeals, was a dispensing of such drugs to a bona fide patient with an injury, to relieve pain. Whether the drugs were delivered on the first and fourth or the third and fourth days of the month was not important. The defendant physician should not be made to enter a felon's cell simply because a woman's unsupported memory disagreed with his recollection, corroborated by his written record as to the dates

he served her in her distress. In the judgment of the court the drugs had been dispensed in good faith by a physician in the course of his professional practice under conditions under which, as provided in the Harrison Narcotic Act, a written order is not necessary. The dispensing of narcotic drugs by a physician to a patient does not constitute a violation of section 1044(a) of the Harrison Narcotic Act.

Although the defendant's entries in his records under the name of "G. Hagen" do not truly reflect what happened, there was, said the court, an actual illness on the part of a Mrs. Whalen and a bona fide delivery of narcotic drugs to her for treatment of her ailment, as the law permits. Had there been no injury or illness and no patient and had the government been in some manner cheated, there might be cause for complaint. However, continued the court, when, as in the instant case, there is a record of narcotic drugs dispensed to sick persons who need and actually receive such drugs, resulting in the alleviation of their suffering, then we go far afield in an attempt to enforce the law by blasting the future of a professional man on such evidence. The law requires that a verdict of guilty be based on more than merely some evidence; it demands that it be based on substantial evidence. In this case the substantial evidence was as consistent with innocence as with guilt. The evidence failed to support the charge that the defendant had unlawfully sold narcotic drugs to persons unknown. The making of false records did not raise a presumption, as the government assumed, that the narcotic drugs falsely recorded were sold by the defendant to some one else. The defendant could still have the narcotic drugs or he could have dispensed or administered them not unlawfully in the course of his professional practice.

In the judgment of the appellate court the trial court should have directed a verdict of acquittal, because there was no substantial evidence of a violation of the law. The appellate court held further that the trial court had committed an error prejudicial to the defendant when it admitted in evidence the testimony of a witness for the government that two individuals who had been sentenced for drug addiction had been seen to visit the defendant's office on various occasions. The court also censured the prosecution for its improper cross examination of a physician imputing a narcotic charge to the witness, who had testified as a character witness for the defendant. Accordingly, the circuit court of appeals reversed the judgment and remanded the case.—*Towbin v. United States*, 93 F. (2d) 861.

Workmen's Compensation Acts: Services of Medical Expert Witnesses Not "Medical Services."—The workmen's compensation act of Louisiana requires the employer to furnish to injured employees "reasonable medical, surgical and hospital services." In a proceeding under that act a workman requested that five medical expert witnesses, whom he had hired to examine him and testify at the trial, be paid their fees of \$25 each, because their services constituted "medical services" within the meaning of the act. In denying the workman's request, the Supreme Court of Louisiana said that "medical services" as used in the workmen's compensation act refers to medical services in the nature of attention and treatment administered to injured employees and not to the services of medical expert witnesses called for purposes of litigation.—*Jones v. Hunsicker et al.* (La.), 177 So. 576.

Society Proceedings

COMING MEETINGS

- American Society of Tropical Medicine, Oklahoma City, Nov. 15-18.
- Dr. E. Harold Hinman, Wilson Dam, Ala., Secretary.
- Central Society for Clinical Research, Chicago, Nov. 4-5. Dr. Lawrence D. Thompson, 4932 Maryland Ave., St. Louis, Secretary.
- D. Thompson, 4932 Maryland Ave., St. Louis, Secretary.
- Inter-State Postgraduate Medical Association of North America, Philadelphia, Oct. 31-Nov. 4. Dr. W. B. Peck, 27 East Stephenson St., Freeport, Ill., Managing Director.
- Pacific Coast Society of Obstetrics and Gynecology, Los Angeles, Nov. 30-Dec. 3. Dr. T. Floyd Bell, 400 29th St., Oakland, Calif., Secretary.
- Radiological Society of North America, Pittsburgh, Nov. 28-Dec. 2. Dr. Donald S. Childs, 607 Medical Arts Bldg., Syracuse, N. Y., Secretary.
- Southern Medical Association, Oklahoma City, Nov. 15-18. Mr. C. P. Loranz, Empire Bldg., Birmingham, Ala., Secretary.
- Southern Surgical Association, White Sulphur Springs, W. Va., Dec. 6-8. Dr. Alton Ochsner, 1430 Tulane Ave., New Orleans, Secretary.
- Western Surgical Association, Omaha, Dec. 2-3. Dr. Albert H. Montgomery, 122 South Michigan Blvd., Chicago, Secretary.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1928 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but may be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

Alabama State Medical Assn. Journal, Montgomery

8: 97-132 (Sept.) 1938

Brucellosis (Undulant Fever): A Public Health Problem. Alice C. Evans, Washington, D. C.—p. 97.

Early Surgical Intervention in Acute Cholecystitis. R. A. Hamrick, Birmingham.—p. 98.

*Study of Blood Bromide. Georgia L. Johnson, foreword by W. D. Partlow, Tuscaloosa.—p. 105.

Obstructions of Ureter. A. L. Atwood, Birmingham.—p. 107.

Blood Bromide.—In the Bryce Hospital Laboratory, according to Johnson, a quick and simple qualitative test for blood bromide is done by dropping 0.5 per cent solution of acid brown gold chloride into tubes containing serums left over after the complement fixation test has been set up. Familiarity with the changes in color produced in the presence of bromide in the serum enables one to pick up relatively small quantities of bromide—even as low as 25 mg. per hundred milliliters of blood. The serums showing an appreciable amount of bromide are subjected to a quantitative analysis. The principles of the method involve the preparation of a protein free filtrate by coagulation with trichloroacetic acid, and the addition of the gold chloride solution to the filtrate producing changes in color (due to the formation of gold bromide) varying from a yellowish brown to a reddish brown. This corresponds to the concentration of bromide. A high proportion of persons having nervous and mental disorders are given bromide more or less as a routine. Toxic symptoms develop in a little more than one out of five (based on 1,243 tests). The more widespread use of a quantitative test for bromide in the blood in all hospitals and clinics will result in a better knowledge of bromide therapy and a more complete understanding of its misuse.

American J. Digestive Diseases, Huntington, Ind.

5: 405-460 (Sept.) 1938

Vitamins in Relation to Gastrointestinal Diseases. M. G. Vorhaus, New York.—p. 405.

Studies on Parallel Action of Vitamin C and Calcium. S. L. Ruskin, New York.—p. 408.

Passage of Gallstones Through the Sphincter of Oddi. Marie Ortmayer and Margaret Austin, Chicago.—p. 411.

Infra-Red Photography of the Abdominal Wall in Portal Cirrhosis of the Liver. I. R. Jankelson and H. Baker, Boston.—p. 414.

Efficiency of Several Germicides and Antiseptics on Oral Mucosa. Esther Meyer and L. Arnold, Chicago.—p. 418.

Primary Carcinoma of the Liver. A. Levitt and D. S. Levy, Buffalo.—p. 420.

*Use of Hydrated Magnesium Trisilicate in Peptic Ulcer: Preliminary Report. M. Kraemer, Newark, N. J.—p. 422.

Variations in Level of Serum Lipase in Experimental Pancreatitis. II. Baxter, S. G. Baxter and J. E. McIntosh, Montreal.—p. 423.

Cod Liver Oil per Rectum as an Adjunct in Treatment of Ulcerative Colitis. R. R. Best, Omaha.—p. 426.

Relationship of Diet to Self Regulatory Defense Mechanism: I. Hydrogen Ion Concentration and Bacterial Flora. N. P. Sullivan and I. A. Manville, Portland, Ore.—p. 428.

Health and Nutrition of High Andean Indians. C. W. Lieb, New York.—p. 432.

Hydrated Magnesium Trisilicate in Peptic Ulcer.—Kraemer has used hydrated magnesium trisilicate in the treatment of thirty-eight patients having roentgenologically proved duodenal ulcers associated with definite hyperacidity to a test meal and typical symptoms. The drug has been used by the

patients for from three to six months. The patients were ambulant. They received three light meals daily and a glass of milk, milkshake or tea between meals and in the evening. One hour after meals and one hour after the between meal feedings and at bedtime they were given a teaspoonful of the powder. Some bromide or phenobarbital was given if there was excessive nervousness or sleeplessness. Some of the patients also received tincture of belladonna. If there was nocturnal pain the patients set their alarm clocks one hour before the anticipated period of distress and took a teaspoonful of the powder at that time. Some of the patients had had recurrences of symptoms for many years and had had many types of treatment. The symptoms of all the patients improved. In order to control psychic factors the patients were not told that they were receiving a new preparation. Intestinal habits were not affected. The author believes that the compound merits further trial.

American J. Obstetrics and Gynecology, St. Louis

36: 363-544 (Sept.) 1938. Partial Index

Fetal Respiration in Relation to Atelectasis and Intra-Uterine Pneumonia. F. F. Snyder and M. Rosenfeld, Baltimore.—p. 363.

Visceral Allergy. J. R. Goodall and R. M. H. Power, Montreal.—p. 372.

*Evaluation of Sedimentation Test in Differential Diagnosis of Acute Pelvic Inflammatory Disease and Acute Appendicitis. C. Lintgen and K. Fry, Philadelphia.—p. 393.

The Management of Breech Deliveries: Based on Report of 709 Cases from the Philadelphia Lying-in Hospital. R. W. Mohler, Philadelphia.—p. 400.

The Cold Pressor Test in Pregnancy. W. J. Dieckmann, H. L. Michel and P. W. Woodruff, Chicago.—p. 408.

Heart Disease Complicating Pregnancy: Study of 436 Cases. H. J. Stander, New York.—p. 413.

Infant Mortality at the Cook County Hospital Among 16,000 Deliveries. D. S. Hillis and S. J. Benensohn, Chicago.—p. 427.

Activation of Uterine Muscles by Estrin and Its Relation to Uterine Growth. S. R. M. Reynolds, Brooklyn.—p. 437.

*Surgical Treatment of Dysmenorrhea. J. C. Masson and Rosemary Shoemaker, Rochester, Minn.—p. 441.

Hyperemesis Gravidarum: Clinical Study of 396 Cases. J. E. Fitzgerald and Augusta Webster, Chicago.—p. 460.

*Relationship of Oral Thrush to Vaginal Mycosis and Incidence of Each. P. W. Woodruff and H. C. Hesselstine, Chicago.—p. 467.

Study of 738 Cases of Uterine Bleeding in Conditions Other Than Pregnancy. F. Weintraub, Brooklyn.—p. 476.

Maternal Intrauterine Hemorrhage Complicating Labor. H. L. Moskowitz and H. Schneider, New York.—p. 489.

Pathologic Properties of Meconium. W. H. Rubovits, E. Taft and F. Newwelt, Chicago.—p. 501.

Aplasia of Lower Female Genital Tract. C. A. Elden, Rochester, N. Y.—p. 507.

Segmental Torsion of Fallopian Tube in a Young Virgin. S. A. Wolfe and D. Kuperstein, Brooklyn.—p. 509.

Sedimentation Test in Inflammatory Diseases.—In determining the value of the sedimentation test as a diagnostic aid in differentiating between acute pelvic inflammatory disease and acute appendicitis Lintgen and Fry performed the test on thirty patients with pelvic inflammatory disease and 100 patients with acute appendicitis. In 90 per cent of the thirty patients with acute pelvic inflammatory disease, the sedimentation of the erythrocytes was more rapid (between 11 and 40 mm. in one hour) than normal. In 52 per cent of the patients with acute appendicitis, the sedimentation rate was abnormal but not as rapid as in the acute pelvic inflammatory group. The authors do not agree with the reports of some observers that the sedimentation rate is never abnormal in acute appendicitis unless rupture or abscess formation has occurred; on the other hand their observations are quite in accord with those of others in regard to the sedimentation rate in acute pelvic inflammatory disease. Their conclusion is that the test by itself cannot be relied on to differentiate between the two conditions, since in practically half of the patients suffering with acute appendicitis sedimentation was abnormal.

Surgical Treatment of Dysmenorrhea.—Masson and Shoemaker sent follow-up letters to 128 patients who underwent operation for the relief of dysmenorrhea. Thirty-four patients were not heard from; therefore the state of the patient's health is known one or more years after operation in ninety-four. Frequently one or more surgical procedures (resection

of the presacral nerve, dilation and curettage, hysterectomy and the like) were done at the one operation, depending on the pathologic condition which was present. Complete relief was experienced by twenty-nine patients, some benefit was obtained by forty-three patients, and twenty-two of the patients did not experience any relief. Fourteen patients in whom hysterectomy was performed still complain of some pain which can be attributed to a tender ovary in some of them. The only procedure that produced uniformly poor results was the insertion of the Baldwin tube, but this procedure has since been discarded.

Oral Thrush and Vaginal Mycosis.—In order to determine the relationship of the sporadic cases of oral thrush in the newborn to vaginal mycosis in the mother, and the general incidence of each, Woodruff and Hesseltine carried out routine vaginal cultures on 402 women in the third trimester of pregnancy. Also ninety babies with positive oral thrush were studied with relationship to mycoses in their mothers. The incidence of fungi in the genital tract of the mothers appears to be associated with the economic and hygienic level. Babies born of such infected mothers have about a thirty-five times greater chance of developing oral thrush than infants born of noninfected mothers. The incidence of fungi in the vaginal tract was 28 per cent. Indigent Negro patients show an incidence of 41 per cent, indigent white patients an incidence of 33 per cent, while the more hygienic class of white patients shows an incidence of 14 per cent. Among 14,640 consecutive babies delivered at the Chicago Lying-in Hospital the incidence of oral thrush was found to be 0.6 per cent (ninety cases). However, in the last 6,130 babies of this total number the incidence of oral thrush was about 1 per cent. This apparent increase is believed to be the result of more careful observations.

American Journal of Ophthalmology, St. Louis

21: 963-1082 (Sept.) 1938

- Biologic Frontal Flaps in Ophthalmology. J. F. S. Esser, Monaco.—p. 963.
- *Effects of Oxygen Deprivation on the Central Visual Field. J. N. Evans, Brooklyn, and R. A. McFarland, New York.—p. 968.
- Evaluation of Orthoptic Training for Aviators. A. H. Schwichtenberg, Dayton, Ohio.—p. 980.
- Inflammatory Pseudotumor of the Orbit: Report of Case. P. M. Lewis, Memphis, Tenn.—p. 991.
- Chloroma: Report of Case with Hematologic Study. A. D. Frost, Columbus, Ohio.—p. 997.
- Applied Mechanics of Cataract Extraction. E. Jackson, Denver.—p. 1011.
- Papillary Type of Beal's Conjunctivitis. P. Thygeson, New York.—p. 1017.
- The Use of Paredrine in Cycloplegia. I. S. Tassman, Philadelphia.—p. 1019.
- Evaluation of Visual-Testing Methods in Schools: Preliminary Report. J. B. Hitz, Milwaukee.—p. 1024.

Oxygen Deprivation and Visual Fields.—Evans and McFarland conclude from thirty-six experiments on eight eyes of four subjects under conditions of oxygen deprivation that (1) central visual acuity remained unaffected, even at the peak of oxygen deprivation; (2) the angioscotoma widened progressively with progressive oxygen deprivation until it obliterated the visual field, except for a region of from 8 to 10 degrees about the macula; (3) there seemed to be no relation between the minor changes occurring in the blood pressure and the angioscotoma, and (4) there was a marked variation in the extent and rate of widening of the angioscotoma, not only between individuals but also to a lesser degree in one eye as compared to the other eye of the same individual. By placing a patient under the stress of oxygen deprivation, latent defects in the retina may become apparent. In numerous conditions associated with venous stasis, widening defects of the angioscotoma identical in form and extent to those created in the present experiments have been eradicated by the administration of drugs—ephedrine sulfate—which cause vasoconstriction and a rise of blood pressure. The administration of similar medication might be used to overcome the visual and cerebral effects of anoxia in aviators.

American Journal of Physiology, Baltimore

123: 543-808 (Sept.) 1938. Partial Index

- Effects of Intra-Arterial Epinephrine on Blood Flow in an Extremity. N. W. Roome, Chicago.—p. 543.
- Acid-Base Balance of Blood Serum in Hyperthermia. W. H. Danielson, R. M. Stecher, E. Muntwyler and V. C. Myers, Cleveland.—p. 550.
- Observations on Creatinine and Urea Clearances, on Responses to Water Ingestion and on Concentrating Power of Kidneys in Normal, Diabetes Insipidus and Hypophysectomized Dogs. H. L. White and P. Heinbecker, St. Louis.—p. 566.
- Influence of Thyroid Gland on Absorption in Digestive Tract. T. L. Althausen and M. Stockholm, San Francisco.—p. 577.
- Effects in Man and Dogs of Massive Doses of Insulin on Composition of Blood Serum. A. Keys, Minneapolis.—p. 608.
- Influence of Vascular Factors on Mean Pressure, Pulse Pressure and Phasic Peripheral Flow. C. J. Wiggers, Cleveland.—p. 644.
- Study of Circulatory Failure of Adrenal Insufficiency and Analogous Shocklike Conditions. W. W. Swingle, W. M. Parkins, A. R. Taylor and H. W. Hays, Princeton, N. J.—p. 659.
- Effect of Adrenal Cortical Hormone on Circulatory Collapse of Adrenalin Shock. W. M. Parkins, W. W. Swingle, A. R. Taylor and H. W. Hays, Princeton, N. J.—p. 668.
- Vitamin A Reserve of Fur Bearing Animals. A. D. Holmes, F. Tripp and G. H. Satterfield, Raleigh, N. C.—p. 693.
- *Normal Antithrombin of Blood and Its Relation to Heparin. A. J. Quick, Milwaukee.—p. 712.
- Renal Clearances of Iopax, Neo-Iopax and Skiodan in Man. W. W. Smith and H. A. Ranges, New York.—p. 720.
- Effect of Bilateral Ligation of Lumbo-Adrenal Veins on Course of Pancreas Diabetes. H. E. Himwich, J. F. Fazekas and S. J. Martin, Albany, N. Y.—p. 725.
- Experiment in Human Dietary Night-Blindness. G. Wald, H. Jeghers, Boston, and J. Arminio.—p. 732.

Antithrombin of Blood and Heparin.—Quick presents evidence which strongly supports the idea that the antithrombin action of the blood is due mainly to serum albumin. By means of simple but essentially quantitative methods it has been possible to demonstrate that a solution of serum albumin exhibits an antithrombin action remarkably similar to serum itself. It seems fairly certain that serum albumin is not a single substance and therefore it is probably more correct to say that perhaps a constituent of the albumin fraction is responsible for the antithrombin action.

Annals of Otol., Rhinol. and Laryngology, St. Louis

47: 577-864 (Sept.) 1938. Partial Index

- The Problem of Intranasal Medication. T. E. Walsh and P. R. Cannon, Chicago.—p. 579.
- Explanation of Respiratory Failure Sometimes Occurring After a Successful Tracheotomy. V. E. Negus, London, England.—p. 608.
- Psychiatric Therapy in Dysphemia and Dysphonia: Stuttering, Psychophonia, Aphonia, Falsetto. J. S. Greene, New York.—p. 615.
- Tracheal Stenosis from Roentgen Therapy. L. H. Clerf and F. J. Putney, Philadelphia.—p. 666.
- Underlying Factors Concerned in Otitic Hydrocephalus. H. L. Williams, Rochester, Minn.—p. 670.
- Limitations of Bronchoscopy in Treatment of Tracheobronchial Tuberculosis. M. C. Myerson, New York.—p. 722.
- Osteoma of Maxillary Sinus. A. G. Rawlins, San Francisco.—p. 735.
- *Hiatal Hernia. H. J. Moersch, Rochester, Minn.—p. 754.
- Diagnosis and Treatment of Ménière's Disease. S. H. Mygind and Dida Dederding, Copenhagen, Denmark.—p. 768.
- Sinus Thrombosis: Part IV. Venous Thrombosis: Thrombosis of Superior Cerebral Vein. C. W. Irish, Los Angeles.—p. 775.
- Spontaneous Cerebrospinal Rhinorrhea. S. A. Friedberg, Chicago, and T. C. Galloway, Evanston, Ill.—p. 792.
- Consideration of Some of the Causative Factors of Vegetal Bronchitis. F. T. Hill, Waterville, Maine.—p. 814.
- Treatment of Tuberculous Tracheobronchitis. F. W. Davison, Danville, Pa.—p. 826.

Hiatal Hernia.—Esophageal hiatal diaphragmatic hernias have been divided by Åkerlund into three types: (1) congenital short esophagus with partial or complete thoracic stomach, (2) esophageal hiatal hernia without short esophagus and in which the esophagus does not form a part of the hernia; that is, para-esophageal hernia, and (3) esophageal hiatal hernia in which the esophagus is shortened but in which the distal portion of the esophagus is a part of the hernial contents. Moersch bases the present study on 267 cases of diaphragmatic hernia encountered at the Mayo Clinic from 1932 to 1937, 246 of which were of the hiatal type, in contrast to fifteen traumatic and six congenital diaphragmatic hernias other than the hiatal type. Of these, 133 were in women and 113 in men. The average age of the patients was 55 years; the youngest patient was 8 years of age and the oldest 82. All but nineteen of the patients had clinical symptoms that could be directly attributable to the hernia. It was impossible, from the clinical

history alone, to distinguish between the three types of hiatal hernia. The esophagoscopic observations in cases of congenital short esophagus with intrathoracic stomach are a short esophagus with narrowing of the esophagogastric junction and the presence of a dilated portion below this point lined with gastric mucosa, with no evidence of the normal diaphragmatic hiatus. The sliding type of esophageal hiatal hernia may resemble closely the congenital short esophagus with intrathoracic stomach. The esophagus in the sliding type, however, is usually more redundant and the point of narrowing of the esophagogastric junction is less pronounced and shorter. Erosion and ulceration may occur in these cases as well as in cases of congenital short esophagus and may lead to difficulty in differential diagnosis. Bleeding is a frequent accompaniment of esophageal hiatal hernia. When this is present, esophagoscopy is advisable in determining whether or not ulceration and erosion are present. Carcinoma at the cardia at times may offer a great deal of difficulty in diagnosis roentgenographically, and this is especially true when associated with esophageal hiatal hernia. The possibility of a foreign body becoming lodged at the point of obstruction and obscuring the true underlying condition must be considered. The problem of treatment in cases of esophageal hiatal hernia is dependent on the type of hernia and the severity of symptoms. Treatment is not indicated in cases in which there is an absence of symptoms or in which the symptoms are of mild character. When the condition is due to a congenitally short esophagus with intrathoracic stomach dilatation of the narrowing at the esophagogastric junction usually will be sufficient. If definite stenosis is not present at the esophagogastric junction and, especially, if there is an absence of ulceration, the condition may not be a true short esophagus, although the roentgenologic and esophagoscopic observations would seem definite. In cases of other types of hernia, if the symptoms are severe, surgical repair is the procedure of choice. The postoperative results of repair of esophageal hiatal hernia are, as a rule, gratifying. Sixty-four of the 246 patients were subjected to operation.

Archives of Ophthalmology, Chicago

20: 359-540 (Sept.) 1938

- Intra-Ocular Tension in Cases of Sarcoma of Choroid and Ciliary Body. J. H. Dunnington, New York.—p. 359.
- *Clinical Significance of Retinal Changes in Leukemia. G. G. Gibson, Philadelphia.—p. 364.
- Bilateral Congenital Ectopia Lentis with Arachnodactyly (Marfan's Syndrome). J. Laval, New York.—p. 371.
- Nature and Management of Heterophorias. J. T. Maxwell, Omaha.—p. 375.
- Optic Nerve as Diagnostic Sign. D. Vail, Cincinnati.—p. 384.
- Research Studies of the Eye: Some Technical and Practical Notes. A. Busacca, São Paulo, Brazil.—p. 395.
- Advantages of Use of Coagulants in Ocular Operations, Especially in Extraction of Cataract and in Plastic Operations. A. Busacca, São Paulo, Brazil.—p. 406.
- Rotation of the Cheek in Ophthalmology. J. F. S. Esser, Monaco.—p. 410.
- Biochemistry of the Lens: XII. Studies on Glutathione in Crystalline Lens. L. Rosner, C. J. Farmer and J. Bellows, Chicago.—p. 417.
- Retinitis Proliferans: Clinical and Histologic Studies. Bertha A. Klien, Chicago.—p. 427.
- Studies of Visual Fields in Cases of Verified Tumor of the Brain. D. Kravitz, Brooklyn.—p. 437.
- Binocular Vision and Orthoptic Procedure. Dorothy J. Shaad, New York.—p. 477.

Retinal Changes in Leukemia.—Gibson presents the results of a study of the retinal changes and the laboratory observations in twenty-two cases of leukemia. The ophthalmologic diagnosis and prognosis of leukemia are discussed and attention is directed to the close parallelism between the amount of hemorrhage in the retina and the degree of anemia which is associated with the leukemia. Confirmation of the parallelism was furnished by examination of three patients who on first observation had no retinal hemorrhages and only a mild degree of anemia. Subsequently, retinal hemorrhages developed and this development was associated with an appreciable decrease in the number of red blood cells. This decrease was out of proportion to the degree of the clinical hemorrhagic phenomenon. It seemed to make no difference whether the leukemia was of the myelogenous or of the lymphatic type. There is a similar but less consistent correlation between the

hemoglobin and the retinal hemorrhages. It seems that therapeutic and investigative procedures could be more advantageously directed toward the factor of anemia instead of toward the leukocytosis in the unsolved problem of leukemia.

Archives of Otolaryngology, Chicago

28: 313-496 (Sept.) 1938

- Evolution of Speech Organs of Man. V. E. Negus, London, England.—p. 313.
- Diseases of Ventricle of Morgagni, with Special Reference to Pyocoele of Congenital Air Sac of Ventricle. A. O. Freedman, Montreal.—p. 329.
- Cancer of Laryngopharynx. H. B. Orton, Newark, N. J.—p. 344.
- *Pathologic Differentiation Between Radiosensitive and Nonradiosensitive Malignant Neoplasms of the Larynx. W. Harris and P. Klemperer, New York.—p. 355.
- Hemolytic Streptococcus Meningitis of Otic Origin: Report of Recovery. P. Sacks, New York.—p. 364.
- Spontaneous Hemorrhage into Maxillary Sinus. Sobisca S. Hall and H. V. Thomas, Clarksburg, W. Va.—p. 371.
- Lympho-Epithelioma (Schmincke Tumor). W. M. Fitzhugh Jr., San Francisco.—p. 376.
- Influenza with Simultaneous Bilateral Spontaneous Pneumothorax and Subcutaneous Emphysema: Report of Case, with Comment on Mechanism of Production. A. H. Neffson and J. G. M. Bullowa, New York.—p. 388.
- Congenital Dermoid Cyst and Fistula of Dorsum of Nose: Report of Case. E. W. Hagens, Chicago.—p. 399.
- Bilateral Acoustic Neurofibromas. W. M. Craig and E. J. Steenrod, Rochester, Minn.—p. 404.
- Paralysis of Inferior Oblique Muscle Following Caldwell-Luc Operation. J. N. Novick, Washington, D. C.—p. 412.
- Paranasal Sinuses. S. Salinger, Chicago.—p. 418.

Radiosensitive and Nonradiosensitive Neoplasms.—Harris and Klemperer observed thirty-two successive cases of laryngeal carcinoma in which the only treatment was roentgen irradiation (Coutard). In the same period they studied two sarcomas of the larynx and one cylindroma, which also were treated by roentgen rays. All of the lesions occurred on the epiglottis or within the larynx. Twenty of the thirty-two patients responded favorably to the roentgen therapy. Twelve failed to respond. The biopsy material was studied histologically to determine criteria for a pathologic differentiation of radiosensitive and radioresistant neoplasms. The grade of cellular differentiations, mitotic count, anaplasia of the cells, reaction in the stroma and location of the neoplasms were carefully considered. Observations tend to show that there are no pathologic criteria, except possibly for the number of mitoses, which permit of a differentiation between radiosensitive and radioresistant laryngeal carcinomas if protracted fractional roentgen therapy is used. This conclusion seems to contradict the accepted belief that radiosensitivity depends to a great extent on the degree of differentiation of the tumor cells.

Archives of Physical Therapy, Chicago

19: 529-592 (Sept.) 1938

- Psychologic Aspects of Physical Therapy. W. C. Menninger and B. L. Shifflet, Topeka, Kan.—p. 533.
- Evaluation of Treatment of Peripheral Vascular Disease by Alternating Positive and Negative Pressure. R. P. Sturr, Philadelphia.—p. 539.
- Physical Therapy in Internal Medicine: Comments on Its Merits and on Extension of Its Use. P. Irving, New York.—p. 543.
- Ionization of Allergic Rhinitis. E. D. King, Cincinnati.—p. 546.
- Postural Education. J. E. Malcomson, Detroit.—p. 548.
- Common Causes of Failure from Colonic Therapy. J. W. Wiltzie, Birmingham, N. Y.—p. 554.
- Clinical Examination of Labyrinthine Reflex by Galvanic Faling Reaction. E. J. Blonder, Chicago.—p. 561.
- Fulguration of Contact Ulcers of the Vocal Cords. R. E. Howard, Cincinnati.—p. 564.
- Biologic Action of X-Rays and Radiosensitivity. H. Bordier, Lyon, France.—p. 567.

Delaware State Medical Journal, Wilmington

10: 189-204 (Sept.) 1938

- Causes and Treatment of Uterine Bleeding. B. M. Anspach, Philadelphia.—p. 189.
- *Calcium Therapy in Puerperal Infections. W. J. Cusick, Washington, D. C.—p. 194.
- Combined Oral and Rectal Administration of Paraldehyde During Labor. H. F. Kane, G. B. Roth and T. E. Mandy, Washington, D. C.—p. 197.

Calcium Therapy in Puerperal Infections.—Cusick treated twenty-six patients with puerperal infections without a demonstrable cause outside of the pelvis in whom the temperature persisted above 101 F. for more than forty-eight

hours. The chief complaint was abdominal pain and tenderness, located in the lower part of the abdomen. Other complaints were frequency and urgency of urination. In fourteen cases the vaginal discharge was putrid. Microscopic examination of the discharge from both the cervix and the urethra was positive for gonococci in two cases and negative in twenty-four. The treatment employed included rest in bed, an ice bag to the lower part of the abdomen, elevation of the head of the bed, fluids in quantity, magnesia magma when necessary and no sedatives, douches or powerful cathartics. One ampule of 10 cc. of the 10 per cent product of the double salt of calcium gluconate and calcium galactogluconate was injected intraglutally and intravenously each day, after the needle of a 20 cc. syringe was inserted into a vein and 10 cc. of blood was withdrawn and permitted to mix with the calcium solution. Calcium gluconate, one heaping teaspoonful three times a day before meals, was given in warm milk. With this treatment the average hospitalization period was fourteen days, varying from a minimum of nine to a maximum of twenty-two days. The pain disappeared in nineteen patients within thirty-four hours, in four in forty-eight hours and in three within seventy-two hours. Rigidity of the abdomen disappeared in fifty-two hours and tenderness on pressure disappeared within six days. The temperature curve returned to normal within an average of six days. At the time of dismissal the pelvis of all patients were examined and if there was any evidence of an inflammatory process, calcium gluconate was continued orally three times a day.

Georgia Medical Association Journal, Atlanta

27: 337-378 (Sept.) 1938

- Acute Diverticulitis of Colon with Complications: Report of Cases. L. Grove and K. R. Bell, Atlanta.—p. 337.
Altered Mechanics of Supports of the Female Perineum. B. T. Beasley, Atlanta.—p. 344.
Problem Behavior in Children Is Symptomatic. W. W. Young, Atlanta.—p. 348.
Solution of Zinc Insulin Crystals versus Regular Insulin and Protamine Zinc Insulin. H. Bowcock and C. Wilkinson, Atlanta.—p. 351.

Illinois Medical Journal, Chicago

74: 197-288 (Sept.) 1938

- Relation of Allergy to Diseases of Respiratory Tract. T. Nelson, Chicago.—p. 225.
Bronchoscopy in Relation to Diseases of Respiratory Tract. P. H. Holinger, Chicago.—p. 228.
Surgical Treatment of Pulmonary Tuberculosis. W. Van Hazel, Chicago.—p. 232.
Bronchiectasis. D. O. N. Lindberg, Decatur.—p. 235.
Pneumonia in Infancy and Childhood. J. B. Gillespie, Urbana.—p. 239.
Differential Diagnosis of Pulmonary Lesions from Roentgen Standpoint. A. Hartung, Chicago.—p. 243.
*Intradermic Immunization Against Scarlet Fever. C. A. Earle, Des Plaines.—p. 248.
Medical Treatment of Patients with Jaundice. S. A. Portis, Chicago.—p. 249.
Cancer and Precancerous Condition of the Skin. E. A. Oliver, Chicago.—p. 254.
If War Should Come. B. A. Brackenbury, Chicago.—p. 259.
The Field of Activity for the Woman's Auxiliary. I. Abell, Louisville, Ky.—p. 262.
The Management of Carcinoma Patients by the General Practitioner. C. O. Heimdal, Aurora.—p. 265.
Significance in Group Hospitalization Plan. T. J. Lamping, Chicago.—p. 269.
Pregnancy with One Kidney. W. G. Cummings, Winnetka.—p. 274.
Some General Aspects of Modern Therapy in Mental Disorders. P. M. Nation, Anna.—p. 276.
Instance of Hypertension Apparently Due to the Taking of Creosote for a Period of Nine Years. S. K. Robinson, Chicago.—p. 278.
Psychic Impotence. E. W. Hirsch, Chicago.—p. 279.
Nonepidemic Parotitis: Complication of Insulin Shock Therapy. J. W. Klappman, Chicago.—p. 283.

Intradermic Immunization Against Scarlet Fever.—It has been shown that about one tenth of the amount of toxin prescribed by the Dicks, if given into the skin, promises to be as effective as the large amount given subcutaneously and that it is unattended by unpleasant local and general reactions. This smaller amount may be given in three, or perhaps two, divided doses. Since the resulting immunity is probably in proportion to the amount of toxin given, Earle tried increasing amounts: 1,600 skin test doses for the first dose, 4,000 for the second dose and from 8,000 to 10,000 for the third and last dose. He gives

these injections on the outer side of the arm above the elbow. He has now given more than 500 intradermal injections in from 50 to 9,000 skin test doses without unpleasant local or general reactions except in the case of one girl whose temperature rose to 101 F. for a day. At one time he gave fifty-four children three doses, 800, 4,000 and 8,000 skin test doses for the respective doses. A retest showed 87 per cent to be negative. Another group of sixty-one children were given 1,600, 4,000 and 8,000 skin test doses with the same result. Sufficient time has not elapsed to say how long the immunity resulting from intradermal injections will last. In all probability it will last for years. It is possible that a person actively immunized against scarlet fever may be less susceptible to other streptococcal infections. This contention is supported by the laboratory study of hemolytic streptococci which shows that the toxins of many strains are neutralized by scarlatinal antitoxin and are so nearly related that they cannot be differentiated qualitatively by any known test.

Journal of Immunology, Baltimore

35: 155-244 (Sept.) 1938

- *Studies on Mechanism of Action of Sulfanilamide: III. Effect of Sulfanilamide in Serum and Blood on Hemolytic Streptococci in Vitro. J. S. Lockwood, with technical assistance of Helen M. Lynch, Philadelphia.—p. 155.
Specific Protective Property of Serum from Rats Infected with *Cysticercus Crassicolis*. D. H. Campbell, Chicago.—p. 195.
Specific Absorbability of Protective Antibodies Against *Cysticercus Crassicolis* in Rats and *Crassicolis Pisiiformis* in Rabbits from Infected and Artificially Immunized Animals. D. H. Campbell, Chicago.—p. 205.
Quantitative Studies of Complement Fixation Reaction with Syphilitic Serum and Tissue Extract: Technic of Practical Quantitative Test. A. Wadsworth, F. Maltaner and Elizabeth Maltaner, Albany, N. Y.—p. 217.
Studies in Scarlet Fever Immunity. H. Plummer, Toronto.—p. 235.

Mechanism of Action of Sulfanilamide.—Lockwood suggests that blood containing peptone and sulfanilamide may be bactericidal. When peptone is excluded by washing the inoculum in serum or saline, sulfanilamide in the concentration similar to those occurring in the serums of treated patients will completely inhibit multiplication of young streptococci in serum, and sterility will frequently result within twenty-four hours if the inoculum is less than 5,000 chains per cubic centimeter. Smears of the serum after sterilization has occurred suggest that lysis of the majority of the inoculated organisms has taken place. The population curve in any medium is a resultant of the combined activities of peptone and sulfanilamide, with these two reagents exercising opposing effects. Sulfanilamide appears to prevent the specialized metabolic activity required of invasive organisms. The evidence indicates that this effect may be achieved through prevention of the utilization of the protein substrate by the organisms.

Journal of Investigative Dermatology, Baltimore

1: 235-312 (Aug.) 1938

- Effects of Hydrogen Ion Concentration, Fatty Acids and Vitamin C on Growth of Fungi. S. M. Peck and H. Rosenfeld, New York.—p. 237.
*Formalized Herpes Virus Therapy and Neutralizing Substance in Herpes Simplex. S. B. Frank, New York.—p. 267.
Laughlin Test for Syphilis: Description of Certain Modifications, and Clinical and Serologic Comparison with Kline Test and Four Complement Fixation Methods. C. R. Rein and Clarise E. Hazay, New York.—p. 283.
The Capillaries of the Skin: Review. E. M. Landis, Philadelphia.—p. 295.

Herpes Virus Therapy in Herpes Simplex.—Frank treated fourteen patients suffering from recurrent herpes simplex with herpes virus inactivated by formaldehyde and studied quantitatively the antibody response (i. e., the neutralizing titer of the blood serum) to its intramuscular injection and to natural infection. Thirteen patients showed an increase in the interval between attacks and a decrease of severity of the individual attacks. However, none of these patients experienced a complete remission. The recurrences following therapy were abortive and were characterized by the appearance of one, two or three vesicles, which would dry in from twenty-one to forty-eight hours, the crusts being gone in from two to four days. There was no change in the neutralizing titer in the blood serums collected before, during, following and

between attacks. Samples of blood collected from four patients who received the herpes virus were tested and showed no change in the neutralizing titer in spite of the clinical improvement experienced by these patients. Three samples of blood from six individuals who never had herpes showed the presence of the neutralizing substance and three did not. In contrast to this, the serums collected from twenty-two patients who had had herpes all possessed the neutralizing property.

Journal of Nutrition, Philadelphia

16: 209-308 (Sept.) 1938

- Riboflavin Content of Meats. W. J. Darby and P. L. Day, Little Rock, Ark.—p. 209.
- Further Studies on Dietary Factors Associated with Nutritional Muscle Dystrophy. S. Morgulis, Violet M. Wilder and S. H. Eppstein, Omaha.—p. 219.
- Effect of High Glucose and High Fructose Diet on Body Weight and on Fat, Glycogen and Nitrogen Content of Liver and Body of Albino Rat. G. Bachmann, J. Haldi, W. Wynn and C. Ensor, Emory University, Ga.—p. 229.
- Comparative Effects of High Glucose and High Fructose Diet on Activity, Body Weight and Various Constituents of Liver and Body of Albino Rat Exercising at Will. J. Haldi, G. Bachmann, C. Ensor and W. Wynn, Emory University, Ga.—p. 239.
- Egg-Replacement Value of Proteins of Cereal Breakfast Foods, with Consideration of Heat Injury. J. R. Murlin, E. S. Nasset and M. Elizabeth Marsh, Rochester, N. Y.—p. 249.
- Multiple Nature of Deficiency of Blacktongue-Producing Diets as Shown by Studies on Rats. O. M. Helmer and P. J. Fouts, Indianapolis.—p. 271.
- Effect of Riboflavin on Incidence of Curled Toe Paralysis in Chicks. E. L. R. Stokstad and P. D. V. Manning, Petaluma, Calif.—p. 279.
- Fatty Livers in Vitamin B₆ Deficient Rats. Nellie Halliday, Rochester, N. Y.—p. 285.
- Effect of Roughage on Calcium Balance in Rats. W. H. Adolph, C. H. Wang and A. H. Smith, New Haven, Conn.—p. 291.
- Comparison of Ferrous and Ferric Iron in Nutrition of the Rat. E. J. Underwood, Madison, Wis.—p. 299.

Journal of Pediatrics, St. Louis

13: 303-454 (Sept.) 1938

- Recognition of Coarctation of Aorta (Adult Type) During Childhood. G. Eisenberg, Chicago.—p. 303.
- Relation Between Plasma Ascorbic Acid Concentration and Diet in the Newborn Infant. R. L. Mindlin, Boston.—p. 309.
- Vitamin C Content of the Blood in Newborn Infants. A. W. Fleming and H. N. Sanford, Chicago.—p. 314.
- Incidence of Hemolytic Streptococci in Tonsils of Children as Related to Vitamin C Content of Tonsils and Blood. A. D. Kaiser and Betty Slavin, Rochester, N. Y.—p. 322.
- Vitamin C in Tuberculosis: Effect of Supplemeotary Synthetic Vitamin C on Urinary Output of This Vitamin by Tuberculous Children. T. S. Bumbalo and W. W. Jetter, Buffalo.—p. 334.
- Evaluation of Serologic Tests for Congenital Syphilis, with Special Reference to Neonatal Period. J. A. V. Davies, Boston.—p. 341.
- *Diphtheritic Polyneuritis: Report of Nine Cases. J. M. Arena and L. P. Rasmussen, Durham, N. C.—p. 352.
- *Treatment of Meningococcic Meningitis: Intraspinal Use of Antimeningococcus Serum at Bellevue Hospital, 1928 to 1936. N. W. Bolduan, Forest Hills, N. Y.—p. 357.
- Gaucher's Disease in Early Infancy: Review of Literature and Report of Case with Neurologic Symptoms. A. J. Aball and K. Kato, Chicago.—p. 364.
- Treatment of Gonorrheal Vaginitis with Corbus-Ferry Gonococcus Filtrate. L. E. Goldberg, Newark, N. J., and K. Blanchard, East Orange, N. J.—p. 381.
- Celiac Disease and Its Ultimate Prognosis. S. V. Haas, New York.—p. 390.

Diphtheritic Polyneuritis.—During 1937 twenty-five children with diphtheria were admitted to Duke Hospital, nine of whom had polyneuritis due to their infection. The patients were all seen late, and local as well as generalized paralysis had developed. Six of the nine children on whose condition Arena and Rasmussen report had such mild attacks of diphtheria that they were not recognized as such and therefore not treated. The three treated children received only 10,000 units of diphtheria antitoxin late in the course of the disease, one as late as the sixteenth day. Of the nine children, three were referred to the hospital with a diagnosis of acute anterior poliomyelitis, two as having a brain abscess and one with Bell's palsy; the remaining three were diagnosed correctly. Two of the nine children died with myocardial failure. Seven recovered in from one to four months.

Intraspinal Serum in Meningococcic Meningitis.—Bolduan records the results of the intraspinal use of antimeningococcus serum in 191 patients from infancy to 12 years of age,

seen from 1928 through 1936 at Bellevue Hospital. During the years 1928 to 1932 the majority of the patients received serum intraspinally once every twenty-four hours, while from 1932 to 1936 serum was given intraspinally every twelve hours until definite improvement ensued. The criteria for discontinuing serum therapy were decrease of spinal fluid pleocytosis to about 500 cells or less, normal or rapidly falling blood leukocytosis, rising spinal fluid sugar and persistent negative spinal fluid culture. If the foregoing criteria had not been attained after four or five days, a change in the type of serum was made, often with a beneficial outcome. There were forty-eight deaths. This includes one patient who died of a secondary streptococcic meningitis and eighteen patients who received either no treatment (postmortem diagnosis) or who died within twelve hours of the initiation of therapy. Complications developed in from 35 to 40 per cent of the patients (arthritis, otitis media, mastoiditis, nerve deafness, ophthalmitis and blindness). In 1928 and 1929 about 155 cc. of serum was used per patient and in 1935 and 1936 this average was 165 cc. Of forty-eight patients who between 1928 and 1936 received serum by the intravenous as well as by the intraspinal route (usually from 20 to 30 cc. intravenously) ten died. Of those who did not receive serum intravenously there were thirty-eight deaths among 143 patients. The case fatality for 1935 and 1936 of forty-six patients with but three deaths (7 per cent), compared to twenty-two deaths (23 per cent) of ninety-four patients, is ample confirmation of the author's faith in the orthodox method of therapy. During 1928 and 1929, of eighty patients who survived one week, sixty-eight stayed in the hospital longer than two weeks. In 1935 and 1936, of forty-three patients who survived one week, only twenty-five stayed longer than two weeks. In seeking a cause for the reduction in the case fatality rate and in the period of hospitalization from 1928 through 1936 it was felt at first that the administration of serum at intervals of twelve hours was largely responsible. However, two other possibilities had to be considered; a change in the virulence of the organism and an increase in the potency of the serum used. However from figures obtained from the New York City health department the organisms responsible for the 1935-1936 outbreak were quite as virulent as those in 1928 and 1929. Therefore a part of the reduction in case fatality must be ascribed to an increase in the potency of the serums used. Nevertheless, the interval between doses contributed in part to the reduction of mortality.

Journal of Pharmacology & Exper. Therap., Baltimore

63: 353-478 (Aug.) 1938

- *Sulfanilamides in Tertian Malaria. W. E. B. Hall, St. Joseph, Mo.—p. 353.
- Toxicity of Some Organic Selenium Compounds. A. L. Moxon, H. D. Anderson and E. P. Painter, Brookings, S. D.—p. 357.
- Pharmacology of Some New Local Anesthetics. A. R. McIntyre and R. F. Sievers, Omaha.—p. 369.
- Effect on Intestinal Motility of Cyclopropane Anesthesia Alone and After Morphine-Scopolamine Premedication. W. Weisel, W. B. Youmans and W. H. Cassels, Madison, Wis.—p. 391.
- Further Studies on Mechanism of Peptone Shock. C. A. Dragstedt, F. B. Mead and S. W. Eyer, Chicago.—p. 400.
- Effect of Para-Aminobenzenesulfonamide on Oxygen Consumption of Tissue and Certain Pathogenic Bacteria. H. I. Chu and A. B. Hastings, Boston.—p. 407.
- Effect of Morphine on Skin and Rectal Temperatures of Dogs as Related to Thermal Polypnea. A. Hemingway, New Haven, Conn.—p. 414.
- Antianesthetic Effects of Some Convulsants in the Albino Mouse. A. M. Hjort, E. J. De Beer and D. W. Fassett, Tuckahoe, N. Y.—p. 421.
- Some Tetrahydroisoquinolines. III. Relative Antianesthetic Effects. A. M. Hjort, E. J. De Beer and D. W. Fassett, Tuckahoe, N. Y.—p. 432.
- Bulbocapnine-Benzedrine Antagonism. E. Spiegel, Philadelphia.—p. 438.
- Further Studies on Absorption of Mercurial Diuretics as Influenced by Theophylline and Other Substances. R. A. Lehman and A. Dater, New York.—p. 443.
- Trichlorethanol, Tribromethanol, Chloral Hydrate and Bromal Hydrate. G. Lehmann and P. K. Knoefel, Louisville, Ky.—p. 453.

Sulfanilamides in Tertian Malaria.—Hall used sulfanilamides in four consecutive cases of tertian malaria after chills had been well developed in the course of dementia paralytica therapy. Prontosil (prontosil soluble) and sulfanilamide were given separately and in combination while in vitro cultures were made. Chills, with characteristic malarial blood cycles,

continuing in patients receiving sulfanilamide compounds over periods of fifty, seventy, seventy-three and more than 112 hours, indicated that the agents have no effect on tertian malaria within these intervals, nor does further administration to the point of possible effect on the parasite appear advisable. When one considers that prompt response is the primary governing factor in the choice of therapeutic agents, quinine supplemented by atabrine or plasmochin in indicated resistant cases remains as a quickly acting and satisfactory drug in the treatment of malaria. The sulfanilamides do not have a place in tertian malaria, according to the experiments, except as conjectured agents in persistently resistant forms of malaria.

Medical Annals of District of Columbia, Washington

7: 269-306 (Sept.) 1938

Criteria for Early Diagnosis of Cancer of Stomach with Critical Analysis of Value of Flexible-Tube Gastroscopy. F. A. J. Geier, Washington.—p. 269.

A Program for the Prevention of the Common Communicable Diseases. P. W. Gard, Washington.—p. 279.

Saddle Thrombus at Bifurcation of Aorta: Report of Case Treated Conservatively. W. R. Morris, Washington.—p. 285.

Raynaud's Disease. E. J. C. Hildenbrand, Washington.—p. 287.

Hopeful Trends in the Management of Deafness. V. R. Alfaro, Washington.—p. 289.

Minnesota Medicine, St. Paul

21: 601-670 (Sept.) 1938

Phases of Bronchoscopy and Esophagoscopy of Importance in General Practice. V. J. Schwartz, Minneapolis.—p. 601.

Use of Pedicle Muscle Grafts in Facilitating Obliteration of Large, Chronic, Nontuberculous, Pleural Empyema Cavities. H. K. Gray, Rochester.—p. 608.

Acute Upper Respiratory Infections with Gastrointestinal Symptoms. E. D. Anderson, Minneapolis.—p. 611.

Solitary Diverticulitis of the Cecum. W. N. Graves, Duluth.—p. 615.

Fundamentals in Surgical Treatment of Colon Disorders. L. M. Larson, Minneapolis.—p. 617.

Practical Physiology of the Nose. H. I. Lillie, Rochester.—p. 621.

Syncope. B. T. Horton, L. M. Eaton and L. S. Meriwether, Rochester.—p. 628.

*Exfoliative Dermatitis as a Manifestation of Monocytic Leukemia (Schilling). H. Montgomery and C. H. Watkins, Rochester.—p. 636.

Artificial Impregnation. R. T. Seashore, Duluth.—p. 641.

Modern Treatment of Burns: Evaluation of Various Methods Used in 968 Cases in the Cook County Hospital. K. A. Meyer and J. L. Wilkey, Chicago.—p. 644.

Exfoliative Dermatitis in Monocytic Leukemia.—In the last six months of 1937, Montgomery and Watkins encountered four additional cases (two were reported previously) of monocytic leukemia of Schilling associated with exfoliative dermatitis. In these latter cases, changes in the blood may have preceded changes in the skin. It is becoming increasingly apparent that cutaneous manifestations, and especially exfoliative dermatitis, are frequent in monocytic leukemia; about 50 per cent of the cases reported by others have been associated with specific or nonspecific cutaneous lesions. This is in contrast to the relative rarity of specific cutaneous lesions associated with myelogenous leukemia. Purpuric, hemorrhagic and bullous lesions are frequently encountered early in the course of monocytic leukemia, in contrast to their usual appearance as a terminal manifestation in cases of other forms of lymphoblastoma. They may result from specific infiltrations of the skin. Ulcerative gingivitis and bleeding of the gums, which appear to be frequent manifestations of monocytic leukemia, were not associated with exfoliative dermatitis in the authors' six cases. The development of ulcers and furuncle-like lesions is usually a late or terminal manifestation of the disorder. The histopathologic picture of exfoliative dermatitis remains that of the original benign dermatosis or lymphoblastoma causing the exfoliative dermatitis, although it may not be specific as to the type of lymphoblastomatous involvement. The treatment of monocytic leukemia of Schilling is only palliative and consists of high voltage roentgen therapy or radium therapy if the condition is not too acute. Moderate rather than intensive dosage usually gives the best results. The cutaneous lesions frequently involute temporarily, after superficial local roentgen therapy, or indirectly as the result of systemic high voltage roentgen therapy. In acute leukemia treatment is of no avail.

New Orleans Medical and Surgical Journal

91: 111-162 (Sept.) 1938

Relationship of Dentistry to Medicine. H. A. Gaudin, New Orleans.—p. 111.

History of Ophthalmology and Otolaryngology in America, with Special Reference to Louisiana and Mississippi. C. A. McWilliams, Gulfport, Miss.—p. 112.

Acute and Chronic Bacillary Dysentery: Their Relationship to Many Obscure Forms of Colitis and Enteritis. J. Felsen, New York.—p. 114.

Recent Progress in Diagnosis and Treatment of Gastric and Duodenal Ulcer. A. L. Levin and M. Shushan, New Orleans.—p. 120.

Use of Camphor in Oil to Check Lactation. E. C. Smith, New Orleans.—p. 127.

Some Observations on Use of Urinary Antiseptics. J. G. Pratt, New Orleans.—p. 130.

Observations on Insulin and Metrazol Therapy at Central Louisiana State Hospital. S. J. Phillips, Pineville, La.—p. 135.

New York State Journal of Medicine, New York

38: 1151-1204 (Sept. 1) 1938

The History of Public Health. J. R. Earp, Albany.—p. 1151.

Cirrhosis Arrested in a Diabetic Following Insulin Therapy: Report of Case. J. F. Hart and J. R. Lisa, New York.—p. 1158.

Bromsulphalein Test: Checked with Liver Histology. L. Bauman and Louise Orr, New York.—p. 1161.

Primary Papillary Carcinoma of Ureter: Nephro-Ureterectomy. M. E. Greenberger and A. J. Greenberger, New York.—p. 1162.

Controllable Elements in Infant Mortality. F. A. Kassebohm and M. J. Schreiber, New York.—p. 1165.

Tardy Diagnosis of Tumors Affecting the Spinal Cord. W. P. VanWagenen and J. Rossier, Rochester.—p. 1169.

Rheumatic Fever: Relationship of Preceding Infection, Tonsillectomy and Mode of Onset. B. H. Archer, New York.—p. 1177.

Fascial Plastic Operation for Repair of Old Rupture of Rectus Femoris Muscle. M. S. Burman, New York.—p. 1183.

Mucocele of Appendix: Simulating a Neoplasm of the Cecum. I. Kross, New York.—p. 1185.

Pick's Syndrome. H. L. Frosch, New York.—p. 1186.

38: 1205-1256 (Sept. 15) 1938

Mortality of Acute Appendicitis: Analysis of 186 Surgical and Sixty-Nine Nonsurgical Deaths. U. Maes and Elizabeth M. McFetridge, New Orleans.—p. 1205.

Bronchopleural Cutaneous Fistula: Report of Two Cases Treated with Pedicle Flap from Latissimus Dorsi Muscle. I. E. Siris, Brooklyn.—p. 1213.

*Rheumatoid Arthritis: Treatment with Sting of Honeybee. Edith E. Nicholls, New York.—p. 1218.

Arthritis: Relationship of Dental Infection. S. Selig, New York.—p. 1221.

Diphtheria: Susceptibility in a Well Immunized Community. C. H. Maxwell, B. L. Cullen and R. J. Thomas, Auburn.—p. 1227.

Zigzag Method in Insulin Therapy of Schizophrenia. Ruth M. Wilmanns and M. Hayman, Sykesville, Md.—p. 1232.

Unusual Case of Rhinophyma. J. D. Whitham, New York.—p. 1233.

Agranulocytosis: Following Administration of Arspenamines and Bismuth: Report of Case. A. T. Mays, Brooklyn.—p. 1234.

Rheumatoid Arthritis.—Nicholls treated twenty-seven patients with active rheumatoid arthritis with bee stings. The patients had previously received various forms of treatment without beneficial results. Forms of treatment supplementary to the stings of the honeybee were limited to a minimum. An unrestricted diet high in vitamins was usually recommended. Acetylsalicylic acid was frequently prescribed for the relief of pain, and patients were advised to apply heat to the affected joints. All stings were administered by the beekeeper. The site selected depended on the location of the most painful joints. The initial dose was one bee sting. If no reaction followed, the number was increased to three stings at the next visit. The treatment was continued at weekly intervals, the number of stings being increased at each visit. If itching of the skin or any general reaction developed the number of stings was decreased or the treatments were discontinued. Five patients had to discontinue treatments after a few weeks because of severe local or general reactions. Two stopped because they found the treatments disagreeable. Twenty patients continued with the treatment for from three to eighteen months and received from fifty-three to 1,434 stings. Three of the patients were markedly improved and remain well one year later; five were slightly improved; five remained the same, and seven became much worse. Eleven patients experienced severe itching for a few weeks, a generalized maculopapular rash

developed in four, an increase in the joint pains occurred the day following the stings in seven and four experienced severe headache.

Northwest Medicine, Seattle

37: 271-306 (Sept.) 1938

- Cancer of Cervix. R. E. Watkins, Portland, Ore.—p. 274.
Appendectomy in General Practice. W. F. Howard, Pocatello, Idaho.—p. 278.
Hyperplastic Tuberculosis of Cecum and Appendix: Report of Case. C. E. Littlehales, Aberdeen, Wash.—p. 280.
White Blood Count and Sedimentation Rate in Various Stages of Appendicitis. M. S. Rosenblatt and R. H. Humphreys, Portland, Ore.—p. 283.
Gout. J. M. Bowers, Seattle.—p. 284.
Vitamin C and Chronic Arthritis. K. K. Sherwood, Seattle.—p. 288.
Cause of Syncope in Patients with Hypersensitive Carotid Sinus: Report of Case. L. Patricelli, Seattle.—p. 290.
Nausea and Vomiting of Pregnancy: Management. D. J. Thorp, Seattle.—p. 294.
Marked Eosinophilia: Case. H. B. Currin, Klamath Falls, Ore.—p. 296.
Less Common Manifestations of Allergy. J. E. Stroh, Seattle.—p. 297.
Plantar Wart: Case Report. W. Kelton, Seattle.—p. 299.

Ohio State Medical Journal, Columbus

34: 961-1084 (Sept.) 1938

- Clinical Use of Sulfanilamide and Its Derivatives, with Special Reference to Their Possible Toxic Effects. P. H. Long, Baltimore.—p. 977.
The Hearing Problem: A Challenge to Medicine. C. E. Kinney, Cleveland.—p. 982.
Indications for Surgical Treatment of Cholecystitis and Cholelithiasis. C. H. Lenhart, Cleveland.—p. 987.
Early Diagnosis and Care of Pregnancy. H. E. McClenahan, Youngstown.—p. 991.
Hereditary Factors in Growth and Development. A. J. Bell, Cincinnati.—p. 996.
Postpartum Fever. W. K. Gregg, Dayton.—p. 1001.
Prevention and Treatment of Neurosyphilis. N. Michael, Columbus.—p. 1004.
Goiter Heart. J. L. DeCoursey, Cincinnati.—p. 1006.
Importance of Rectal Examination. R. I. Brashear, Columbus.—p. 1008.
Instructions to Mothers on Infant Care. J. W. Larcomb, Columbus.—p. 1009.
Acute Perforation of the Gallbladder. W. W. Stone and F. M. Douglass, Toledo.—p. 1012.

Oklahoma State Medical Assn. Journal, McAlester

31: 295-332 (Sept.) 1938

- Mottled Enamel in Oklahoma Panhandle and Its Possible Relation to Child Development. J. A. Blue, Guyton.—p. 295.
*Recurrent Iritis in Undulant Fever with Concurrent Rheumatic and/or Arthritic Disease. J. R. Reed and E. Goldfain, Oklahoma City.—p. 302.
Undulant Fever: Correlation with Fatigue and Low Grade Fevers. Eleonora L. Schmidt and Elizabeth Dorsey, Norman.—p. 304.
Chronic Gonorrhea. J. H. Howe, Ponca City.—p. 306.
Acute Gonorrhea. R. H. Akin, Oklahoma City.—p. 309.
Necessity of Careful Eye Examinations. D. M. K. Thompson, Muskogee.—p. 312.

Recurrent Iritis in Undulant Fever.—Reed and Goldfain state that chronic brucellosis may be an etiologic factor in the causation of ocular disease, especially iritis. One should carry out tests for undulant fever properly and intelligently when the other more common causes of disorders of the eye have been searched for and not found. Five cases are reported with rather similar histories and changes in that each patient either is suffering from arthritis or has suffered from a rheumatic disease syndrome. Each patient also presented ocular symptoms (recurrent iritis), some of which have been serious. Strongly positive cutaneous reactions were present when tests with the undulant fever organism were made. In addition to strongly positive cutaneous reactions, they yielded a positive opsonic index for undulant fever, indicating active infection when considered in connection with the cutaneous test. Some of them also had positive agglutination tests. In accordance with the criteria of Huddleson, a diagnosis of positive chronic undulant fever infection was established because the opsonic index test revealed phagocytosis in mild, moderate or marked degree of less than 60 per cent and because of the presence of a positive cutaneous test in all five cases, plus a positive agglutination test in four of the cases. While the authors cannot state conclusively that the ocular symptoms were caused by the chronic undulant fever, they feel that it is quite probable in the presence of the unmistakable serologic and immunologic cutaneous reactions for brucellosis.

Pennsylvania Medical Journal, Harrisburg

41: 1083-1296 (Sept.) 1938

- Jejunal Feedings Following Operations on Stomach and Duodenum in Malnourished Patient. J. B. Mason, Philadelphia.—p. 1083.
Management of the Common Cold. H. H. Perlman, Philadelphia.—p. 1086.
The Common Cold from the Standpoint of the Otolaryngologist. N. S. Weinberger, Sayre.—p. 1089.
Treatment of Fracture of the Shaft of the Femur, with Special Reference to Russell and Skeletal Traction. W. L. Estes Jr. and D. P. Walker, Bethlehem.—p. 1092.
Gout Among Arthritics. A. Cohen, Philadelphia.—p. 1100.
The Subconjunctival Cataract Operation. J. B. Feldman, Philadelphia.—p. 1104.
Antenatal and Intrapartum Care of the Fetus. T. L. Montgomery, Philadelphia.—p. 1108.
Management of the Newborn. E. L. Bauer, Philadelphia.—p. 1114.
Relief of Intractable Pain by Subarachnoid Injection of Alcohol. C. H. Harney and H. N. Kehres, Bryn Mawr.—p. 1117.
The Public Relations Policy of the Medical Profession. R. S. Reeves, Philadelphia.—p. 1123.
Treatment of Skin Malignancy by Irradiation. H. W. Jacox, Pittsburgh.—p. 1126.
Role of Renal Infections in Mechanical and Neurogenic Obstructive Uropathies. J. C. Birdsall, Philadelphia.—p. 1130.
Milk Allergy in Children. S. C. Copeland and J. P. Kcating, Philadelphia.—p. 1133.
The March of Events in Pediatrics. T. O. Elterich, Pittsburgh.—p. 1137.
Chronic Pemphigus: Dermatoneurologic Study. A. Strickler and A. Gordon, Philadelphia.—p. 1140.
Pyogenic Liver Abscess. E. L. Eliason, R. B. Brown and D. P. Anderson, Philadelphia.—p. 1147.
Pediatric Problems Related to Cerebrohydrodynamics. T. Fay, Philadelphia.—p. 1154.
Serum Phosphatase as an Aid in Diagnosis of Metastasis of Cancer to the Liver. D. R. Meranze, T. Meranze and M. M. Rothman, Philadelphia.—p. 1160.

Radiology, Syracuse, N. Y.

31: 261-390 (Sept.) 1938

- Roentgen Visualization of Pulmonary Arterial Circulation in Autopsy Material. C. C. Birkelo and W. L. Brosius, Detroit.—p. 261.
Radiotherapy for Tumors of the Testis. E. T. Leddy and A. U. Desjardins, Rochester, Minn.—p. 293.
*Detection of Crystalline Silica in Lung Tissue by X-Ray Diffraction Analysis. H. C. Sweany, Rosalind Klaas, Chicago, and G. L. Clark, Urbana, Ill.—p. 299.
Dosage Chart for X-Ray Therapy. Edith H. Quimby, New York.—p. 308.
Effect of Filtration on Divergent Beams at Supervoltages. Henrietta S. Hayden, K. E. Corrigan and B. Cassen, Detroit.—p. 312.
Attenuation and Transition Effects in Absorption of Supervoltage Radiation. B. Cassen, K. E. Corrigan and Henrietta S. Hayden, Detroit.—p. 319.
X-Rays and Biopsitome in Study of Corpus Uteri. B. H. Orndoff, Chicago.—p. 325.
Discussion of Generalized Osteosclerosis: Report of Unusual Case. P. C. Swenson and G. G. Holzman, New York.—p. 333.
Further Observations Concerning Recovery of Lost Radium. R. B. Taft, Charleston, S. C.—p. 340.
Anomalies of Clavicle, with a Previously Unreported Variation. C. Liebman and N. B. Freedman, Montreal.—p. 345.
*X-Ray Studies on Effect of Opium on Gastrointestinal Tract in Man. E. H. Fell, Chicago.—p. 348.
Development of High Voltage X-Ray Tubes at the California Institute of Technology. C. C. Lauritsen, Pasadena, Calif.—p. 354.

Crystalline Silica in Lung Tissue.—Sweany and his collaborators subjected samples of lung tissue from a wide variety of cases to x-ray diffraction analysis. Previous to the chemical analysis the tissues had been hardened in a dilute solution of formaldehyde, dried in vacuo at 70 C., ground to pass a 40 mesh sieve and dried further to constant weight at from 105 to 110 C. For the x-ray study thin samples were prepared by packing the powdered tissue into disks from 0.2 to 0.3 mm. in thickness. The x-ray beam, collimated by two 0.01 inch pinholes, was supplied by a tube with a copper target, operating at peaks of 20 milliamperes and 27 kilovolts. The film was held in a flat holder at a distance of 5 cm. from the sample. The exposure time was usually seven hours. The results show that there is a close parallelism between the presence of siliceous fibrosis and the presence of quartz. In several of the cases investigated the pathologic changes were slight and at times doubtful; yet there was sufficient indication that the threshold of danger was approaching. In normal lungs and unexposed lungs the quartz lines were uniformly absent. In some cases the large amount of silica was probably chiefly due to silicates. Application of the technique is still in the

experimental stage. There would seem to be great possibilities for its use, but until further studies have been made caution should be exercised in expecting more than preliminary data would warrant. The method, although sharply specific, is thus far only qualitative. However, in all probability it can be developed on a quantitative or a semiquantitative basis. The authors' experiments have been confined chiefly to lung tissue, with a few analyses on lymph nodes. The determination, therefore, is applicable only to patients who have died. It seems highly probable that results of some value may be obtained from the study of sputum by this method. The method of determination of quartz in mine dust, as described by Clark and Reynolds, has vast possibilities in the evaluation of the hazards of working conditions. No dust analysis should be considered complete without an x-ray diffraction analysis to show when quartz is present, the amount and the size of the particles. The finding of quartz lines in the x-ray diffraction pattern of dried and ground lung tissue indicates the presence of sufficient quartz to produce or to have already produced silicotic fibrosis.

Effect of Opium on Gastrointestinal Tract.—Fell presents the results of repeated gastrointestinal x-ray examinations on three normal subjects conducted during protracted administration of opium. Control observations were carried out on the same subjects at times when they did not receive the drug. There was no characteristic delay in the emptying time of the stomach. An apparent slowing of the barium sulfate in the upper portion of the small intestine was revealed by an increased concentration of barium sulfate in that portion (a feathery appearance). There was no marked delay in the emptying time of the small intestine. An increased rate of motility in the large intestine occurred in only one subject. There was a delay in the emptying time of the ascending colon of from eight to thirty-one hours, and from four to twenty-six hours in the total emptying time of the intestine. Difficulty in expelling stools was experienced in spite of an increased desire to defecate. The action of the ileocecal valve was uninfluenced by opium. Opium caused constipation and small, dry and hard stools. This work suggests that opium produces constipation by causing difficulty in the expelling of the stools rather than direct action on the motility of the gastrointestinal tract. The difficult defecation depends perhaps on the hardness and dryness of the stools or on increased tone of the anal sphincters.

Southern Medical Journal, Birmingham, Ala.

31: 959-1042 (Sept.) 1938

- Some Observations on Repair of Cleft Lip. N. Owens, New Orleans.—p. 959.
- Unusual Secondary Changes in Myoma of Uterus. L. C. Harris Jr. and H. C. Schmeisser, Memphis, Tenn.—p. 968.
- Altered Mechanics of the Female Pelvic Structures. B. T. Beasley, Atlanta, Ga.—p. 976.
- Treatment of Sterility. L. J. Globet, San Antonio, Texas.—p. 981.
- Endometrioma of Umbilicus Following Cesarean Section. G. T. Tyler Jr., Greenville, S. C.—p. 987.
- Giantism: Report of Case. C. D. Humbert, Barnard, Mo.—p. 988.
- Renal and Perirenal Tumors in Children: Report of Two Cases. W. F. Lake and A. J. Ayers, Atlanta, Ga.—p. 992.
- Modern Care of Anorectal Fistula. C. D. Gaston, Birmingham, Ala.—p. 996.
- "Primary" Streptococcal Peritonitis Treated with Sulfanilamide: Report of Case with Recovery. J. S. Horsley Jr. and D. G. Chapman, Richmond, Va.—p. 999.
- Results of Roentgen Therapy in Essential Hypertension. F. P. Boswell, Montgomery, Ala.—p. 1001.
- Diagnosis of Nasal Allergy and Its Relation to Other Manifestations. F. K. Hansel, St. Louis.—p. 1003.
- Syphilis, Malaria and Hookworm Disease as Industrial Hazards in the South. C. F. Holton, Savannah, Ga.—p. 1011.
- Unrecognized Disorders Frequently Occurring Among Infants and Children from the Ill Effects of Milk. W. A. McGee, Richmond, Va.—p. 1016.
- Ulcer Cornea Rodens (Mooren's Ulcer). J. F. Townsend, Charleston, S. C.—p. 1020.
- Human Glands: Case Report. A. A. Herold and C. B. Erickson, Shreveport, La.—p. 1022.
- Research and Graduate Teaching in the Preclinical Departments of Southern Medical Schools. T. P. Nash Jr., Memphis, Tenn.—p. 1022.
- Orthopedic Participation in a Public Program of Care for Crippled Children. A. F. Vostell, Baltimore.—p. 1029.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Journal of Ophthalmology, London

22: 513-576 (Sept.) 1938

World-Wide Distribution of Trachoma, Excluding the Dominions, Colonies and Mandated Territories of Great Britain. A. F. MacCallan.—p. 513.

Withdrawal of Interretinal Fluid in Detachment Operation by Simple Suction Apparatus. C. J. Blumenthal.—p. 542.

*Hydrostatic Approach to Posterior Chamber for Diagnostic and Therapeutic Purposes. A. Motegi.—p. 543.

Hydrostatic Approach to Posterior Chamber.—Motegi used intra-ocular irrigation for the examination and treatment of patients with poor vision in whom the anterior segment of the eye is nearly normal but the fundus is invisible; patients with poor vision, following diseases of the anterior segment peculiar to the tropics, in whom the fundus is invisible, and patients with panophthalmitis. Through an incised wound of the eyeball 0.9 per cent saline solution or Ringer's solution at body temperature is run. The excess solution drops out of the wound. In infected cases this may be followed by autoserum. If the vitreous is fluid, the eye tends to collapse as it exudes. The irrigation restores the globular form of the eye and enables observation of the interior to be made through the incision. If the vitreous is turbid it is easier to see the fundus through the clear saline solution, which replaces it, than through the hazy medium. This method permits removal of foreign bodies and lavage of infective material from the posterior chamber in cases of panophthalmitis with the possibility of cure under direct vision.

Journal of Pathology and Bacteriology, Edinburgh

47: 205-360 (Sept.) 1938

- Production of Homogeneous Suspensions of Vaccinia Elementary Bodies and Histology of Associated Skin Lesions. C. R. Amies.—p. 205.
- Structure of "Rough" and "Smooth" Colonies. K. A. Bisset.—p. 223.
- Antigenic Basis of Tumor Transplantation. P. A. Gorer.—p. 231.
- Diffuse Leptomeningeal Tumor in a Child: Comments on "Sarcomatosis" of Meninges. R. A. Willis.—p. 253.
- *Haemophilus Para-Influenzae Endocarditis. A. A. Miles and J. Gray.—p. 257.
- Estrogens of Testis and of Adrenal in Relation to Treatment of Enlarged Prostate with Testosterone Propionate. C. W. Emmens and A. S. Parkes.—p. 279.
- Mesenteric Chyladenoclasia with Steatorrhea and Features of Addison's Disease. L. E. Glynn and M. L. Rosenheim.—p. 285.
- Histologic Types of Meningiomas and Comparison of Their Behavior in Tissue Culture with That of Certain Normal Human Tissues. J. O. W. Bland and Dorothy S. Russell.—p. 291.
- Atypical Amyloidosis with Macroglossia. W. G. Barnard, F. B. Smith and J. L. Woodhouse.—p. 311.
- Reactivity of Some Diphtheria Prophylactics. P. J. Moloney and M. D. Orr.—p. 315.
- Suprasellar Tumor in Dog. E. G. White.—p. 323.
- Polycythemia Terminating in Leuko-Erythroblastic Anemia. Doris M. Stone and Dorothy Woodman.—p. 327.
- *Sensitivity of Rheumatic Subjects to Streptococcus Products. C. A. Green.—p. 337.

Haemophilus Para-Influenzae Endocarditis.—Miles and Gray describe two cases of infective endocarditis, apparently due to *Haemophilus para-influenzae*. Comparison of these with previously reported cases of "influenza" and para-influenza bacillus endocarditis reveals no significant difference in clinical characteristics, nor do the anatomic or histologic observations distinguish the hearts from others with subacute "influenza" or streptococcal endocarditis. Ulceration, excessive formation of granulation tissue and marked infiltration of the polymorphonuclear cells are conspicuous histologic features in the two cases, but these are not distinctive. The septic nature of the lesion found in some parts conforms with the relatively rapid progress of the disease and, in view of the observed variable duration of "influenza" endocarditis, the septic features do not necessarily indicate a characteristic tissue reaction to hemophilic bacilli. The features of certain reported cases suggest respiratory lesions as the source of the endocardial infection. There is no record of infection of the endocardium with *Haemophilus influenzae* identified by tests in the X and the V medium. All strains of endocarditis to which such tests have been applied have proved to be *Haemophilus para-influenzae*. There are indications that some of the so-called influenza bacillus infections were due to *Haemophilus para-influenzae*.

A systematic description is given of the two strains of endocarditis isolated. They synthesize the X but not the V factor and are identified as *Haemophilus para-influenzae*, nonhemolytic variety. Their characteristics are compared with those of two other strains of endocarditis of *Haemophilus para-influenzae* and of eighteen strains freshly isolated from human sources other than the endocardium and blood. The two strains are serologically related to each other, to one of the endocarditis strains and to two of the eighteen nonendocardial strains. With freshly isolated para-influenza bacilli, fermentation reactions were obtained only in peptone-water sugars enriched with yeast extract. Yeast extract as usually prepared is unsuitable as a source of the V factor for this purpose, as it contains a sucrose-splitting enzyme which is heat stable in acid solution.

Sensitivity of Rheumatic Subjects to Streptococcus Products.—Green states that of thirty-two cases of acute rheumatism, twenty-seven, fourteen and thirteen showed cutaneous sensitivity to endotoxin of autogenous hemolytic, viridans and indifferent streptococci, respectively. Of 105 patients with acute and subacute rheumatism 75 per cent gave positive cutaneous reactions with a stock preparation of hemolytic streptococcus endotoxin as compared with 24 per cent of 105 nonrheumatic controls. In a limited number of quiescent cases, local and general manifestations of the rheumatic syndrome have been induced by subcutaneous injection of hemolytic streptococcus endotoxin. The evidence supports the view that hemolytic streptococcus infection is an important factor in the production of the rheumatic state.

Lancet, London

2: 603-650 (Sept. 10) 1938

- Treatment of Prostatic Obstruction. H. P. Winsbury-White.—p. 603.
Further Experiments on Administration of Hormones by Subcutaneous Implantation of Tablets. R. Deanesly and A. S. Parkes.—p. 606.
Tuberculin Patch Tests in Children. F. D. Hart.—p. 609.
*Effect of Hesperidin (Vitamin P) on Capillary Fragility. H. Scarborough and C. P. Stewart.—p. 610.
*Effect of Induced Hypercalcemia on Excessive Psychomotor Activity. T. M. Cuthbert.—p. 612.
Monarticular Arthritis Associated with Dysenteric Bowel Infection. J. D. Benjafield and G. S. Halley.—p. 616.
Operative Treatment of Labyrinthine Vertigo. M. Yearsley.—p. 618.
Pneumococcal Meningitis Treated with 2-(p-Aminobenzenesulfonamido) Pyridine: Recovery. G. C. K. Reid, with a note by S. C. Dyke.—p. 619.
Pneumococcal Septicemia: Id. S. C. Dyke.—p. 621.
Estimation of Hemoglobin in Undiluted Blood, Using a Lovibond Comparator. G. A. Harrison.—p. 621.

Effect of Hesperidin on Capillary Fragility.—Scarborough and Stewart state that oral administration of hesperidin (vitamin P) reduced the number of hemorrhages in six patients with vitamin deficiency. This effect was observed when petechial hemorrhages were induced by the application of pressure and in spontaneous hemorrhages after the administration of arsenic or bismuth (hemorrhagic capillary toxicosis of Frank). In these cases the effect appears to be independent of the presence of ascorbic acid in the diet.

Hypercalcemia and Excessive Psychomotor Activity.—There is some evidence that when increased nervous excitability exists induced hypercalcemia exerts a sedative effect. Cuthbert induced hypercalcemia in nineteen patients showing increased excitability. Six patients received 4 Gm. of calcium lactate and 6,300 international units of vitamin D daily. The dosage of parathyroid extract was regulated by frequent estimations of the blood calcium, varying from 10 to 110 units. Eleven patients were given 6 Gm. of calcium lactate, 6 ounces (180 cc.) of lactose (an attempt to promote intestinal acidity), 9,400 international units of vitamin D and from 4 to 6 Gm. of ammonium chloride. Injections of parathyroid extract were given every four hours and later every six or eight hours for from three to sixteen days. The efficiency of the medicinal therapy alone, without parathyroid extract, in promoting hypercalcemia was observed in two patients. Eight patients were discharged within nine months of treatment; this is much higher than the hospital discharge-rate for the year. Eight other patients were greatly improved. A good response was obtained in nearly three fourths of the treatments given. The remissions arising with and after treatment were definitely longer than any spontaneous remissions before treatment, with one exception. When the percentage

rise in blood calcium was more than 30 the period of maximal response was generally under ten days; when improvement commenced below this, the maximal response was more prolonged; thus if a rise of from 20 to 30 per cent in the blood calcium is obtained improvement follows. The only undesirable effects observed were drowsiness in one patient on the tenth day and vomiting in another probably due to acidosis. Treatment did not have to be curtailed because of these symptoms. The results suggest that once the parathyroid is stimulated into activity, activity persists for some time—from two to six weeks at least. Treatment was found most effective in the absence of hallucinosis. Some patients became resistant to parathyroid extract after heavy dosage for about twelve days. Results suggest that in treating future cases prolonged intensive medicinal therapy should be tried first; but if a more rapid result is desired parathyroid extract should also be given intramuscularly every four hours, the patient receiving about 150 units daily until improvement begins. The injections may then be given less frequently and smaller doses used. Every effort must be made to utilize the resulting period of remission, and the patient's fullest cooperation should be obtained.

Medical Journal of Australia, Sydney

2: 265-318 (Aug. 20) 1938

- Toxic Goiter, with Special Reference to End Results. A. Newton.—p. 265.
Diagnosis of Poliomyelitis. M. L. Powell.—p. 276.
Infection with *Trichomonas Vaginalis*: Treatment with Silver Picrate. H. G. Furnell.—p. 284.

2: 319-360 (Aug. 27) 1938

- Some Recent Advances in Therapy. A. W. Holmes & Court.—p. 319.
Simple Procedures in Treatment of Painful Feet. B. Keon-Cohen.—p. 325.
Painful Feet. E. E. Price.—p. 332.
The History of Renal Physiology. F. Arden.—p. 335.

2: 361-404 (Sept. 3) 1938

- Factors in Prognosis of Cardiac Disease. A. W. Holmes & Court.—p. 361.
Some Observations on Examination of Men Exposed to Lead Hazard at Mount Isa, Including an Original Method for Examination of Blood for Polychromasia. L. A. Windsor-McLean.—p. 367.
Endemic Typhus in North Queensland. R. Y. Mathew.—p. 371.
*Intrauterine Tuberculin Test of Mantoux: Method Employing a Single Injection. D. Anderson and C. Harvey.—p. 378.

Intracutaneous Tuberculin Test of Mantoux.—Anderson and Harvey devised a single injection technic for the Mantoux test, using purified protein derivative. This was employed in population surveys to detect a high percentage of the total positive reactors with a minimum of untoward reactions. They felt that a smaller injection ought to produce a correspondingly smaller allergic response in a susceptible subject as readily recognizable as that produced by the larger injection of the same strength. Accordingly 123 volunteers, some known reactors and some clinic patients not previously tested, were given into the right arm an injection of 0.005 mg. of tuberculin purified protein derivative in 0.1 cc. of diluent, and into the left arm an injection of 0.00125 mg. of tuberculin purified protein derivative in 0.025 cc. of diluent. The two injections were given at the same time. It was found to be easy to measure the smaller dose with as much or almost as much accuracy as the larger dose. From this experiment it is concluded that an injection of one fourth of the volume of the standard second strength injection of tuberculin purified protein derivative detects all or nearly all the reactors to the Mantoux test. The specificity of the smaller reactions is still unmistakable by the experienced interpreter. The sharper reactions are of substantially less severity. The scheme of dosage of Long, Aronson and Seibert should be followed when practicable, but if only one injection can be given this may safely and effectively consist of 0.00125 mg. of tuberculin purified protein derivative in 0.025 cc. of diluent. An experience of more than 1,000 such injections has shown that, though sharp reactions are relatively frequent, they are practically never large enough to be inconvenient and that the proportion of reactors is as great as with the larger injection. Of the first 500 adult subjects tested with the single injection technic thirty-three had some degree of vesiculation; of these the reaction was large and more or less sore in ten and in five some tenderness was complained of when the reaction was neither large nor vesicular. Only four subjects required treatment, three for blistering and one for itching.

Annales de Dermatologie et de Syphiligraphie, Paris

9: 657-768 (Aug.) 1938

*Vulvar Tuberculosis. J. Gaté and P. J. Michel.—p. 657.
Experimental Studies on Alteration of Cutaneous Reaction in Course of Repeated Irritations of Skin. L. Török with the assistance of D. Kenedy, E. Lehner, E. Rajka and F. Urban.—p. 677.

Vulvar Tuberculosis.—Gaté and Michel follow Bulkley's classification of vulvar tuberculosis. This author differentiated an ulcerous, an ulcerohypertrophic and a purely hypertrophic form but he also mentioned fistulas and abscesses and lupus of the vulva. Following a review of these different types of vulvar tuberculosis, the authors give detailed clinical histories of two cases of their own. In the first case, which concerned a young woman aged 19, the clinical picture suggested a primary tuberculosis. The anamnesis as well as a thorough clinical and roentgenologic examination gave no indication of a preexisting tuberculous infection. The onset of the pathologic manifestations was characterized by an erythema nodosum, which is one of the classic aspects of the primary complex. This erythema nodosum involved the lower extremities. The vulvar ulceration involved the left labium minoris. Moreover, there was an acute and suppurating adenopathy. The source of the tuberculous infection could not be determined. The woman's husband was examined but was found to be in perfect health. The second case of tuberculous ulceration in the region of the vulva concerned a young woman who had been married for seven months and whose husband had died one month after marriage from meningitis, which was probably of a tuberculous nature. The authors further review the clinical history of a case which was first described by Hellerstrom of Stockholm. In this case there existed a tuberculous ulcer of the vulva complicated by a tuberculous adenopathy of the inguinal region. This case is interesting not only because it was of conjugal origin but especially because a venereal lymphogranuloma was at first thought of. In the conclusion the authors emphasize once more the clinical polymorphism of vulvar tuberculosis, pointing out that this explains the occurrence of diagnostic errors. They stress that laboratory tests are helpful in avoiding diagnostic errors.

Journal de Médecine de Lyon

19: 507-526 (Sept. 5) 1938

*Dolichocolon and Painful Abdominal Crises. C. R. Bocca.—p. 507.

Dolichocolon and Painful Abdominal Crises.—Bocca maintains that if a barium enema discloses an elongation of the large intestine and perhaps the presence of curves, bends and S-shaped or figure 8-shaped loops, it is justifiable to affirm the existence of a dolichocolon. According to some authors, a dolichocolon is only a banal roentgenologic aspect without great pathologic significance. However, there are others who regard the dolichocolon as a morbid entity which is usually accompanied by clinical signs such as constipation, aerocoly and painful abdominal crises of a particular character. These painful abdominal crises are of three types: One group has the point of origin outside of the intestine. These patients may complain of dyspeptic disturbances, of hepatobiliary disorders or of pains in the ileocecal region. The second group has painful abdominal crises connected with colitis. Colitis is one of the most frequent complications of dolichocolon and it is especially grave, because its treatment is so difficult. The third group has painful crises of the subocclusive type. The author says that he observed this type of crisis in nine of twenty-nine cases of dolichocolon. In five of these nine cases the symptoms of occlusion concurred with those of colitis, but in the other four cases they existed alone; they had a tendency to recur and to disappear spontaneously. Discussing the complications that may arise from dolichocolon, the author mentions volvulus, adhesions, pericolicitis and vascular complications. Regarding the diagnosis he says that it should be based on roentgenoscopy following an opaque enema. The treatment should be chiefly a medical one. The author mentions dietetic measures and also medicaments to reestablish the normal motility of the intestine. The value of enteroclysis is still in dispute. For the treatment of the abdominal crises, warm compresses and antispasmodics are recommended. The author says that in the noncomplicated cases of dolichocolon many surgeons recommend first a trial with medical treatment. In some complications such as volvulus a surgical intervention is necessary.

Presse Médicale, Paris

46: 1281-1288 (Aug. 24) 1938

*Lungs and Microbes. L. Binet and C. Jaulmes.—p. 1281.
Circumscribed Lipo-Atrophy of Insulinic Origin. L. Cornil.—p. 1282.

Action of Isolated Lung on Micro-Organisms.—Binet and Jaulmes report their investigations on the microbicidal power of the isolated lung, which they carried out during the last two years. After describing their technic of the perfusion of the isolated lung, they state that their microbicidal studies were made with the following micro-organisms: hemolytic streptococcus, Staphylococcus aureus, bacillus of swine erysipelas, bacillus of anthrax, Bacillus pyocyaneus and enterococcus. They found that a lung which is aseptically isolated, rhythmically ventilated and continuously perfused with citrated blood, and which is kept under physiologic conditions as regards temperature and hydration, is capable of exerting an influence on the micro-organisms that are added to the blood of perfusion. The different micro-organisms disappear progressively from the blood that perfuses the lung. The authors think that various factors play a part in this gradual disappearance of the micro-organisms: a hematic factor (action of leukocytes and thrombocytes), a respiratory factor (influence of the composition of air which circulates in the lung) and a pulmonary factor proper. It was further observed that if a suspension of carbon or of india ink was added to the perfusing blood twenty or thirty minutes before the introduction of the micro-organisms, the disappearance of the bacilli from the blood was hindered or at least retarded. This reduction in the microbicidal power, following the introduction of india ink is probably the result of the blockage of the reticulo-endothelial system.

46: 1329-1344 (Sept. 7) 1938

Hemolytic Anemia with Hemoglobinuria and Hemosiderinuria: Case. M. Brulé, P. Hillemand and R. Gaube.—p. 1329.
*New Test of Hepatic Insufficiency: Test of Provoked Levulosemia. R. Rivoire, R. Gayet, A. Bermond and F. Moreau.—p. 1331.

New Test of Hepatic Insufficiency.—Rivoire and his associates suggest a new test for the detection of hepatic insufficiency. It consists in determining in the blood of the patient, at half-hour intervals for a total period of two hours, the degree of levulosemia, after the ingestion of a quantity of levulose, equivalent to 50 cg. per kilogram of body weight. The more accentuated the curve of levulosemia, the greater is the hepatic insufficiency. This test is based on a well known phenomenon, namely the fixation of levulose by the liver (identical or analogous to that of dextrose or galactose); but, whereas the dextrose content of the blood is determined, in addition to the hepatic fixation, by multiple other extrahepatic factors, it appears that these factors have no effect whatever on the levulose content of the blood. This property of levulose has been employed previously in tests on hepatic insufficiency, namely in the provoked levulosuria. However, when the sensitivity of this test did not prove to be superior to provoked galactosuria, it was abandoned in favor of the latter. The authors made fifty tests with provoked levulosemia. They found that outside of hepatic insufficiency only slight variations in the provoked levulosemia curve exist. In fasting persons, no levulose is detected in the blood; at the most, traces are found in some subjects. After ingestion of levulose, it appears in the blood at the end of twenty or thirty minutes and reaches its maximum of from 10 to 15 mg. per hundred cubic centimeters of blood at the end of the first hour, after which it subsides again or reaches less than 6 mg. at the end of the second hour. However, in cases of hepatic insufficiency, the levulosemia reaches 40, 50 or even 60 mg. at the end of the first hour. It is extremely inconstant and in severe cases it may be greatly prolonged so that it is still observable at the end of the third hour, but the authors think that it is the peak of the hyperlevulosemia, which is characteristic for hepatic insufficiency. They admit that this test requires further investigations but they have found that levulosemia is positive in about one of two cases of certain hepatic disorders in which the galactosuria test produces negative results, but they never observed the opposite phenomenon. They conclude that provoked levulosemia is a more sensitive test than are those previously proposed for the detection of hepatic insufficiency.

Revue Neurologique, Paris

70: 1-148 (July) 1938

Hemiballism and the Subthalamus. H. Marcus and H. Sjögren.—p. 1.
Meralgia Paresthetica in Course of Aneurysm of Abdominal Aorta.
A. de Castro.—p. 29.

Role of Hypertonic Solutions in Treatment of Migraine. G. Villey,
J. F. Buvat and Mme. Buvat-Pochon.—p. 32.

Hypertonic Solutions in Migraine.—Villey and the Buvats report the results that they obtained with the intravenous injection of hypertonic solutions of sodium chloride in the course of attacks of migraine. They present a detailed clinical history which suggested to them that the disturbances presented by this patient were related to a paroxysmal attack of intracranial hypertension. Accordingly, they subjected the patient to intravenous injections of hypertonic solution of sodium chloride from the beginning of the painful period of his attack. The pain ceased during the first hour after the injection; the subconfusional condition disappeared within several hours. The authors treated the patient in this manner for a year; at each of their treatments, the pain subsided in from twenty to forty minutes; the effect on the state of confusion varied. They further cite the clinical histories of several other patients who had migraine of a more typical character. The histories indicate that 20 cc. was the dose usually administered by intravenous injection; the concentration of the solution was either 10 per cent or 20 per cent.

Minerva Medica, Turin

2: 133-156 (Aug. 11) 1938

Nervous Forms of Pellagra Cured by Nicotinic Acid. G. Frontali and G. Ferrari.—p. 133.

Dynamic Auxiliary Therapy in Course of Balneotherapy and Luthotherapy in Salt and Iodine Waters. A. Mosetti.—p. 148.

Pellagra.—Frontali and Ferrari administered the nicotinic acid treatment to fourteen adults (men and women) who were suffering from grave forms of nervous pellagra, either primary or recurrent. The disease was of long duration in all cases and had resisted the commonly used antipellagragenic diet and also the polyvitaminic preparations. All the patients had nervous disorders. Three with a demential form of pellagra had some ancestors or relatives with psychoses and pellagra. Seven patients were suffering from amentia and mental depression. Two pellagrous alcoholic patients had delirium and hallucinations. The treatment consisted in daily administration of 160 mg. of nicotinic acid for from thirty to fifty days. Every day 40 mg. of the acid was administered intramuscularly and 120 mg. of the acid was given by mouth. The treatment was given in the course of a pellagragenic diet in four cases and in the course of the common antipellagragenic diet in ten cases. The following results were obtained from the treatment in all cases: (1) complete elimination of the pellagradermal lesions within one or two weeks, (2) restoration of normal function of digestion within from thirty to thirty-three days and (3) slow but constant regression of the nervous symptoms. By the end of the treatment the patients had gained from 5.5 to 8 Kg. Asthenia, hypertonia, paralysis and pain disappeared. As to the mental disorders the treatment failed in dementia. Amentia and mental depression were controlled without residual mental disorders. The authors show the advisability of administering the treatment early in the development of the disease before irreversible changes of the nervous tissues take place. They believe that the results of the treatment are permanent if the patients have an antipellagroid diet for life. Otherwise the administration of a quantitatively sufficient and qualitatively well balanced pellagragenic diet has to be complemented with nicotinic acid for an indefinite time.

Rinascenza Medica, Naples

15: 505-540 (Aug. 15) 1938

Milkers' Nodules: Case. E. de Gregorio and R. de Blasio.—p. 511.

Toxic Action of Aminopyrine on Blood. A. Pouché.—p. 512.

Scoliosis in School Children. A. Curcio.—p. 516.

Toxic Action of Aminopyrine on Blood.—Pouché says that aminopyrine, when administered in a therapeutic dose, may induce leukopenia with hypogranulocytosis. He administered a daily dose of 0.1 Gm. to ten normal infants for ten consecutive

days. He made determinations of the values of the leukocyte on the first, fifth and last days of the treatment. In two of the cases leukopenia with hypogranulocytosis resulted from the treatment. In one of the cases leukocytes and granulocytes, which were 11,200 and 4,200 respectively before administration of aminopyrine, diminished to 5,488 and 462 respectively on the tenth day of the treatment. As the administration of the drug was discontinued, the granulocytes returned to normal values. The author believes that patients who react with leukopenia and hypogranulocytosis to aminopyrine have a special sensitivity to it, and he points out the possible danger in administering the drug.

Rivista di Patologia e Clin. Tuberculosis, Bologna

12: 527-608 (Aug. 31) 1938. Partial Index

Histogenic Reactions of Tuberculous Allergy. E. Frola.—p. 527.

Sodium Acetate in Cultural Differentiation of Tubercle Bacilli of Human and Bovine Types in Petragani's Culture Medium. A. Rosa and R. Maccolini.—p. 539.

Behavior of Fibrinogen in Course of Pulmonary Tuberculosis. M. Anzalone.—p. 545.

**Cavitation and Phthisiogenesis in Children and Adolescents.* E. Filla.—p. 566.

Tuberculous Cavitation of Lung in Children.—Filla reports eighty cases of pulmonary tuberculous cavitation in children ranging in age from 2 to 15 years. The condition is more rare in children before the age of 8 years than in older children. In the majority of the cases the caverns originate in an early tuberculous infiltration of the parahilar or subclavicular zones of the lung. Only in rare cases the infiltration takes place at either the apex or the base of the lung, or it originates in the form of pulmonary tuberculosis other than an early tuberculous infiltration. The exudative and the fibrous forms are the most frequent forms of pulmonary tuberculosis in children. The prognosis is serious. The largest frequency of the development of the disease coincides with sex maturity. The disease is more serious in girls than in boys. Recovery takes place in about 25 per cent of the cases if the diagnosis is made early and the patients are cared for in antituberculous institutions for a long time. When the disease develops in adolescents they rarely reach the adult stage. The author points out the importance of preventing the disease and also of an early diagnosis. He emphasizes the advisability of making repeated systematic clinical and roentgen examinations of the thorax of children at the prepuberal age.

Revista de Tuberculosis del Uruguay, Montevideo

7: 1-110 (No. 1) 1938. Partial Index

**Roentgenogram of Dry Hydatid Cyst of Lung.* O. Ivanissevich.—p. 6.
Recurrent Large Hemoptysis from Remains of Hydatid Cyst of Lung: Immediate Cure After Phrenectomy. L. Muñoz Moratorio and S. Grezzi.—p. 20.

Technic of Lamas and Mondino's Two Stage Operation for Hydatid Cysts of Lung. D. Prat.—p. 28.

Luxation of Azygos Lobe: Treatment by Artificial Pneumothorax. M. S. Olivera.—p. 90.

Roentgen Shadow of Dry Hydatid Cyst of Lung.—Ivanissevich says that there is a sign of value for the roentgen diagnosis of incarcerated dry hydatid cyst of the lung. According to the author, when the fluid of an echinococcus cyst of the lung is spontaneously eliminated, the cystic membrane collapses and becomes incarcerated by the adventitial layer of the lung. The roentgen shadows of uncomplicated hydatid cysts of the lung, as well as of cancer of the lung, are round with dark regular smooth borders when the roentgenograms of the thorax are taken in the anteroposterior and lateral positions. Those of dry incarcerated hydatid membrane of the lung are round when the thorax is taken in the anteroposterior position and polygonal with irregular light borders when a lateral view is made. The small borders of the membrane, which are not imprisoned by the adventitial layer of the lung, project out through one or various bronchial branches. The author believes that the special shadow is due to the different distribution of the planes of clastic tension in the lung in relation to the position of the structure in the thorax as the volume of the lung adapts itself to the conditions of internal collapse of the dry hydatid membrane.

Archiv für Dermatologie und Syphilis, Berlin

178:1-98 (Aug. 20) 1938. Partial Index

- *Eczema in Bricklayers. W. Burckhardt.—p. 1.
 *Chemotherapy of Gonorrhea with Sulfanilamide Compounds, Particularly with Disseptal C (D B 32). H. Felke.—p. 45.
 History of Osler's Disease (Hereditary Hemorrhagic Telangiectasia). A. Fingerland and B. Janoušek.—p. 54.
 Nonhereditary Epidermolysis Bullosa in Cutaneous Amyloidosis. A. Marchionini.—p. 65.
 Clinical Aspects and Pathogenesis of Rare Cutaneous Pustuloses. H. Fuhs.—p. 68.
 Sarcoid-like Cutaneous Tuberculosis Caused by Chicken Tuberculosis. N. Danbolt and Anton Brandt.—p. 76.

Eczema in Bricklayers.—Burckhardt presents an analytic and experimental study of the occupational disease of the skin of bricklayers, the so-called cement-lime eczema or bricklayers' eczema. In studies on the causes of this disorder, simple toxic as well as allergic factors were investigated. Tests were made on eighty patients with bricklayers' eczema and on 100 healthy controls. The patients with bricklayers' eczema had only a slight hypersensitivity to cement, lime and their constituents, but they had a lowered cutaneous resistance and a hypersensitivity to alkaline substances. Tests revealed that cement and lime produce in every person an eczematoid dermatitis and that 90 per cent of the patients with bricklayers' eczema reacted to application of cement or lime with these ordinary toxic reactions. Thus there was no allergic hypersensitivity to cement and lime in 90 per cent of the patients with bricklayers' eczema; they merely had ordinary toxic hypersensitivity to these substances which was the result of their lowered resistance to alkaline substances. Only eight of the patients (10 per cent) responded with eczematous reactions to cement and lime. In seven of these there existed in addition to the bricklayers' eczema seborrheal eczema or obscure endogenous eczemas. Thus there was a possibility that the eczematous reactions developed on the basis of an isomorphic irritation. In only one case did the conditions indicate the existence of a true allergy against alkaline action or against bodies that originate as the result of the toxic effects of these alkaline substances on the skin. The author suggests that besides alkali, the calcium ion plays a part in the toxic action of cement and lime on the skin, because calcium chloride likewise produces eczematoid cutaneous reactions and the concentrated cement and lime suspensions are rich in calcium ions. The author concludes that the diagnosis of bricklayers' eczema should be based chiefly on the anamnesis and the clinical picture. He thinks that the patch tests serve only for more detailed studies. Protection of the skin against massive contact with cement and lime is usually an adequate prophylaxis against bricklayers' eczema.

Chemotherapy of Gonorrhea.—Felke employed three different sulfanilamide preparations (disseptal A [dimethyl disulfanilamide], B [monomethyl disulfanilamide] and C [disulfanilamide]) on 270 patients with gonorrhea. Having found disseptal C, also referred to as D B 32, to be the most effective of the three, he has employed this preparation exclusively since December 1937. He found that a daily dose of 1.5 Gm. (given in three doses of 0.5 Gm. each, at eight hour intervals) produced an average concentration of free D B 32 of from 1 to 1.5 mg. per hundred cubic centimeters of serum. When the concentration reached 2 mg. per hundred cubic centimeters, cyanosis usually resulted. The author adhered to the short term administration; the daily dose of 1.5 Gm. was usually given for six days; that is, 9 Gm. of the medicament was regarded as a therapeutic "thrust." When a second thrust became necessary, the author increased the daily dose to 2 Gm. and continued this dose for four days. He says that in a third thrust, the daily dose may even be increased to 3 Gm. (three days). He explains why this is possible and then describes observations on twenty women with gonorrhea who were treated with daily doses of 1.5 Gm. Discussing these and also sixty-five cases of gonorrhea in men, who were treated likewise with disseptal C, he mentions the importance of the so-called therapeutic maturity. This implies that in order to be effective the chemotherapy should not be begun too early. A summary report of the sixty-five cases of gonorrhea in men indicates that when the medica-

tion with disseptal was begun from the eleventh day on, the treatment was generally more effective than when it was begun before this time. When chemotherapy was begun too early the majority of patients required two or more therapeutic courses, whereas when it was begun later, one course was adequate in the majority of cases. In the conclusion the author states that in men the chemotherapy should be combined with local treatment but that in women such treatment is superfluous, except that in new cases simple vaginal irrigations may be given. The development of an undesirable resistance of the organisms can be prevented by avoiding insufficient doses.

Nervenarzt, Berlin

11: 385-440 (Aug. 15) 1938

- Clinical Aspects of Cerebral Metastases of Carcinoma. K. E. Pass.—p. 385.
 *Epileptiform Attacks in Insulin Therapy of Schizophrenia. Gerty Gross-May.—p. 400.
 *Treatment with Vitamin B₁ in Delirium Tremens. J. Kloster.—p. 413.
 So-Called Reflex Epilepsy. K. Hebel.—p. 415.

Epileptiform Attacks in Insulin Therapy of Schizophrenia.—Gross-May says that of 105 schizophrenic patients who were subjected to insulin therapy, thirty-seven had one or more epileptiform attacks in the course of the treatment. The occurrence of these attacks showed no dependence on the age and sex of the patient and no relation to the dose or type of insulin, to the blood sugar content or to the atmospheric conditions. On the other hand, it cannot be ruled out that epileptic heredity produces a predisposition. However, the author emphasizes in this connection that there are considerable clinical differences between a true epileptic attack and the epileptiform hypoglycemic crisis. Depending on the time of appearance of the attack, she differentiates two groups of patients, those with early and those with late epileptiform attacks. In the first group, the attacks develop between the second and the third half hour after the injection of insulin, in the second group between the second and the fourth hour. In women the relatively early attacks are more frequent, in men the late attacks. Evaluating the therapeutic significance of the epileptiform attacks, the author says that the results are somewhat better in the patients in whom these attacks develop than in those in whom they do not. However, this more favorable prognosis is partly explained by the fact that the duration of the schizophrenia was on the average shorter in the persons who reacted with epileptiform attacks. If an attack is immediately followed by an improvement, the prognosis is favorable. In some cases the attack may be followed by an exacerbation. In cases in which the attacks occur early, the danger of somatic damage is slight, but in the late cases measures should be taken immediately to prevent such damage. If, however, attacks are desired for therapeutic reasons, the insulin shock therapy should be combined with the administration of metrazol.

Vitamin B₁ in Delirium Tremens.—After pointing out that vitamin B₁ is now widely used in the treatment of alcoholic polyneuritis, Kloster says that he tried vitamin B₁ in the treatment of delirium tremens. Following the description of a case in which the intravenous injection of 50 mg. of crystallized vitamin B₁ produced favorable results, he says that vitamin B₁ was employed also in ten patients in whom delirium tremens had not yet completely developed. In three of these patients a surprising improvement was noticeable one or two hours after the injection; the psychic unrest was much improved, and the tremor and the intoxicated appearance were lessened. Moreover, eight of the ten patients slept quietly the first night after the administration of vitamin B₁. Large doses (from 20 to 80 mg.) of a synthetic vitamin B₁ preparation were injected intravenously from one to three times at intervals of an hour. The author further cites another patient with the symptoms of delirium tremens, in whom vitamin B₁ was employed with good results. He realizes that this material is too small to permit a definite evaluation of the treatment of delirium tremens with vitamin B₁, but he hopes that the treatment will be tried by others. He regards the fact that vitamin B₁ apparently causes

no undesirable secondary effects and the fact that as yet there is no thoroughly satisfactory treatment of delirium tremens as additional justification for a trial of the treatment with vitamin B₁.

Zeitschrift für klinische Medizin, Berlin

134: 533-670 (Aug. 8) 1938. Partial Index

Question of Nephrosis. T. Fahr.—p. 533.

Agranulocytosis. K. A. Seggel.—p. 563.

Studies on Normal and Pathologic Physiology of Gastric Movements: Observations on Blood Sugar Level, Gastric Motility and Gastric Disturbances. F. Brauch.—p. 581.

*Angina Pectoris Simplex and Hemodynamic Load of Heart. W. Raab.—p. 595.

*Changes in Blood During Necroses in Cardiac Muscle and in Striated Muscles. W. Hauss and T. Yamanaka.—p. 604.

Value of Roentgenology in Diagnosis of Diseases of Small Intestine. G. Wachner and S. Zollner.—p. 634.

Relations Between Pernicious Anemia, Gastric Polyps and Gastric Carcinoma. G. Velde.—p. 653.

Angina Pectoris Simplex.—Raab applies the term angina pectoris simplex to those forms of typical stenocardiac disorders which are not caused by acute coronary thrombosis, hypertensive crisis or a mitral defect but occur during physical exertions, excitement, after heavy meals, under the influence of low temperatures or even without recognizable causes. The opinion prevailing today is that angina pectoris simplex is the result of a disparity between the cardiac function and the coronary blood perfusion; that is, of an excessive hemodynamic load on a cardiac muscle, the blood perfusion of which is inadequate, because of a stenotic condition in the coronaries. The author concedes that the presence of an excessive hemodynamic load probably plays a part in the majority of cases of angina pectoris but that, on the other hand, it should not be overlooked that increase in blood pressure and in the beat frequency may be absent during the attack and that even the electrocardiographic aspects of hypoxemia of the cardiac muscle may be absent during rest as well as during the work test or during the spontaneous attack. The investigations described in this paper were made to determine whether excessive hemodynamic loads are absolutely essential in the development of stenocardiac symptoms of the type designated as angina pectoris simplex. Summarizing his observations, the author says that in cases of angina pectoris simplex the behavior of blood pressure and pulse frequency, on the one hand, and the appearance of stenocardiac symptoms during a spontaneous attack or after a work test, on the other hand, frequently show no interrelationship. Considerable prolonged improvement or complete disappearance of the symptoms of angina pectoris, for instance after the irradiation of the adrenals, occurs in angina pectoris with hypertonia often without a decrease in the hypertension. In angina pectoris with normal tension and cardiac compensation, the decrease or disappearance of the symptoms is accompanied by a gradual increase in the pressure. Among 130 patients with angina pectoris, there were only 43 per cent in whom the systolic pressure was permanently in excess of 160 mm. of mercury. Thus the author arrives at the conclusion that in many cases of angina pectoris simplex excessive hemodynamic loads on the heart play no part in the pathogenesis.

Blood During Muscular Necrosis.—Hauss and Yamanaka point out that the relations between myocardial necrosis, electrocardiogram and hematologic changes have not been completely explained as yet. In order to gain insight into these relations, the authors made studies on twenty-five patients with myocardial infarct. They watched for changes in the temperature, number of leukocytes, sedimentation speed, blood sugar, rest nitrogen and sodium chloride content of the blood. The values detected by them corresponded largely to those which they found reported in the literature. Discussing the diagnostic and prognostic significance of the observed changes, they state that although fever is of considerable significance for the diagnosis of myocardial infarct it is of no prognostic significance. With regard to the leukocyte count, the conditions are similar. The sedimentation speed is of great diagnostic value because its acceleration generally persists for weeks; that is, as long as

necrotic substances are being absorbed. The authors advise rest in bed until the sedimentation values are normal. Fluctuations in the blood sugar values are of no prognostic significance but an increase in the rest nitrogen content seems to indicate an unfavorable prognosis. In order to determine the causes of the changes, the authors induced small sterile muscular necroses on the thigh of dogs and thus produced fever, acceleration of the sedimentation speed and increases in the leukocyte count, the blood sugar and the rest nitrogen. Since these changes largely resemble those observed in cardiac infarct, the authors think that a resorption of necrotic substances is responsible for these symptoms in patients with cardiac infarct as well. The fact that the entire organism is involved in the reaction is considered to be a result of the vasomotor action of the products of decomposition.

Vestnik Khirurgii, Leningrad

55: 373-514 (April) 1938. Partial Index

Repair of Traumatic Defects of Skin. S. M. Kalmanovskiy and E. L. Zhak.—p. 375.

Role of Anaerobes in Noma. A. M. Geller and T. I. Medvedeva.—p. 380.

Topography of Peripheral Branch of Facial Nerve. A. V. Shilova.—p. 391.

Roentgenologic and Surgical Treatment of Cancer of Breast According to Winz. N. N. Tsachenko, N. N. Sokolov, E. D. Dubovyi and L. E. Korytkin-Novikov.—p. 395.

*Intraperitoneal Adhesions. S. A. Abramovich.—p. 402.

Intraperitoneal Adhesions.—Abramovich produced adhesions in the peritoneal cavity of dogs by various methods such as the introduction into the cavity of sterile foreign bodies, swabbing the serosa with a 5 per cent solution of pepsin, with tincture of iodine or with alcohol, or by scarifying the serosa of an intestine on one or both sides. The abdomen was closed without drainage and a relaparotomy was performed at intervals of from three weeks to four and one-half months. The author found that sterile foreign bodies became encapsulated by adhesions of firm connective tissue and were surrounded by the omentum. The effect of the pepsin solution was to produce delicate, easily separable adhesions. Application of tincture of iodine did not always result in adhesions and such as were formed were delicate and readily separated. Swabbing the peritoneum with alcohol or introducing of small amounts of it (from 5 to 10 cc.) caused the formation of wide and firm adhesions. Scarification of one side did not produce adhesions; when opposed sides in contact with each other were scarified, dense adhesions resulted. The introduction of petrolatum did not prevent the formation of adhesions. Free omental transplant to a defect in the serous covering of the intestine likewise failed to prevent adhesions. The use of a 0.5 or 1 per cent Payr's pepsin-Pregl solution in dividing adhesions resulted in their reformation. The author concludes that there is no substance capable of preventing the formation of adhesions in the peritoneal cavity. He therefore stresses their prophylaxis in the careful handling of the serous surfaces, in careful hemostasis, in avoidance of trauma, in drying the peritoneal surfaces and in the use of tampons and drains. In the postoperative period prophylactic measures consist in encouraging early rising from bed and the early function of the intestine through feeding.

Hospitalstidende, Copenhagen

S1: 773-788 (Aug. 16) 1938

*Calvé-Perthes Disease After Fracture of Neck of Femur in Young Persons and Its Significance for Understanding of Pathogenesis of Aseptic Necrosis of Epiphysis. B. Nielsen.—p. 773.

Calvé-Perthes Disease.—Nielsen reports two cases of Calvé-Perthes disease in boys after fracture of the neck of the femur. He concludes that the most probable cause of this disease after fracture is a lesion of the nerves of the afferent blood vessels. Functional disturbances occur which result in reduced nutrition of the bony tissue and consequent pathologic changes, including increased calcium content. The cases of clearly traumatic origin, he says, do not allow the conclusion

that the necrosis of the epiphysis in other cases is due to trauma. There is evidence that the disorder depends on hereditary anomalies of development; the cause is believed to be connected with the unknown processes which determine normal development. Calvé-Perthes disease with changes in the acetabulum and in the upper part of the neck of the femur is regarded as the result of more extended disorder of the nerves and of the blood vessels. Differences in the blood vessel supply of the epiphysis seem to explain the differences between some of the secondary necroses in adults and those in children.

Nederlandsch Tijdschrift v. Geneeskunde, Amsterdam

82: 3931-4054 (Aug. 13) 1938

- Congenital Passive Immunity. J. J. Van Loghem.—p. 3935.
 Concealed Hyperthyroidism. J. B. Polak.—p. 3940.
 Extensive Gold Dermatitis with Pigmentation Resembling Lichen Ruber Verrucosus After Administration of Gold Preparation. R. Kooij.—p. 3945.
 *New Observations and Studies on Familial Nuclear Anomaly of Leukocytes (Pelger-Huët). S. J. Leitner and P. C. Gugelot.—p. 3953.
 Tuberculosis and Aneurin (Vitamin B₁₂) Metabolism. J. Goudsmit.—p. 3964.
 Treatment of Disturbances of Sexual Function in Males. A. H. Fortanier.—p. 3971.
 Injections of Progesterone as Substitute for Corpus Luteum. W. C. Kors.—p. 3976.
 Primary Chronic Infectious Polyarthritides: Case. J. H. Van Gortel.—p. 3977.

Familial Nuclear Anomalies of Leukocytes.—Leitner and Gugelot direct attention to the nuclear anomaly of the leukocytes which was first described by Pelger in 1930 and the familial nature of which was demonstrated by Huët in 1932. After citing other observers who have made reports on this anomaly, they say that in their own studies on the familial nuclear anomaly of the leukocytes they examined seventeen patients who belonged to three families. The anomaly consists in an inhibition of the segmentation, so that the blood contains only staff-nuclear cells and cells with two-segmented but rarely with three-segmented nuclei. The shape of the nucleus is characterized in the segmented ones by short, plump, round symmetric fragments, connected by a thin chromatin thread, in the staff-nuclear cells by a thinner divided one with thickened terminations. While the nuclear shape is still in a young stage, the structure of the nucleus has all the signs of maturity, namely, high chromatin content, coarse lamella formation or even signs of hypermaturity; that is, pyknosis. This dissociation between the degree of maturity of the shape and structure of the nucleus is the most characteristic aspect of the familial nuclear anomaly of Pelger-Huët. The heredity is dominant and not sex linked. In spite of the fact that tuberculosis occurred in the three families studied by the authors, a direct relation with this or other diseases cannot be detected, because the anomaly has been observed also in entirely healthy families. The examination of the bone marrow revealed that in the Pelger-Huët anomaly not the discharge of cells from the bone marrow is abnormal but rather the formation of the cells. In the sternal punctate the myelocytes and the metamyelocytes are increased at the expense of the staff nuclear and the segment nuclear. The typical nuclear structure is observed occasionally already in the myelocytes but generally in the metamyelocytes. The neutrophil as well as the eosinophil and the basophil elements are involved. The functional test by means of intracutaneous tuberculin injections resulted in a deviation toward the left in the leukocytic blood picture, although to a lesser degree than did the treatment with a bacillary vaccine, the latter causing a great increase in myelocytes and metamyelocytes. Tests on the peripheral and medullary blood disclosed that the cells with mature nucleus phagocytize as severely as do the normal leukocytes of control persons. However, the immature cells from the bone marrow do this inadequately. Consequently, as soon as a strong mobilization of the leukocytes takes place, the defense of the organism may be inadequate. Not only has a knowledge of the anomaly differential diagnostic significance but it is also of scientific interest in that it is the first discovered hereditary anomaly of the leukocytes.

Ugeskrift for Læger, Copenhagen

100: 925-954 (Aug. 18) 1938

- *Erroneously Diagnosed Cranial Tumors. K. H. Krabbe and M. Ellermann.—p. 925.
 Cardiac and Respiratory Neurosis. H. Heckscher.—p. 930.
 Perinephric Abscess with Opening into Bronchus. K. T. Petersen.—p. 937.
 Treatment of Acne Vulgaris Juvenilis with Thyroidin. S. N. Vendel.—p. 939.

Erroneously Diagnosed Cranial Tumors.—Of the eighteen cases of cranial tumors described by Krabbe and Ellermann, fourteen had been diagnosed as vascular diseases of the brain, two as cerebrospinal syphilis, one as epidemic encephalitis and one as disseminated sclerosis. In all necropsy disclosed tumor of the brain, in the last case coincident with the disseminated sclerosis. The authors find that hemiparesis of acute onset in an older person without signs of choked disk may be due to a multiform glioblastoma in a cerebral hemisphere. If the albumin count is more than 20 and the picture nevertheless is that of a thrombosis rather than of hemorrhage in the brain, a tumor may be present, and the probability of a tumor is strengthened if the patient is increasingly dull, exhausted and confused. Multiform glioblastomas, however, are usually inoperable. In cases in which there is meningioma there is a certain intermittence in the symptoms, especially at the start; otherwise there is steady progression. When there are chronic extended cerebral symptoms an intracranial tumor may be probable; in rare cases meningiomas may also have an acute start and rapid course. In syphilitic patients with cerebral symptoms the possibility of a tumor should not be overlooked.

100: 955-988 (Aug. 25) 1938

- Pneumonia Studies: IV. Continued Investigations on Croupous Pneumonia, Especially Concerning Treatment with Pneumococcus Rabbit Serum. N. I. Nissen.—p. 955.
 *Experiences with Serum Treatment of Croupous Pneumonia. W. T. Andersen.—p. 966.
 Cases of Grave Recurrence of Rectal Prolapse. C. C. Fleischer-Hansen.—p. 969.
 *Auscultation of Cranium as Part of Neurologic Examination. T. Dalsgaard-Nielsen.—p. 971.
 Prognosis of Treated Syphilis. E. Lombolt.—p. 975.
 Application of Isotonic Sodium Bicarbonate Solution in Treatment of Diabetic Coma. E. Kirk.—p. 977.
 Allergy and Gastric Ulcer. O. S. Olesen.—p. 978.
 Prescription Sign. H. W. Tetens.—p. 980.

Serum Treatment of Croupous Pneumonia.—In forty-one of sixty patients with acute pulmonary diseases Andersen found pneumococci of different types, most often types I, VII and III. Pneumococci were demonstrated in thirty of the thirty-four patients with croupous pneumonia, and twenty-four were treated with type specific rabbit serum. In the patients with type III the effect was negative or doubtful; in the others good, with a few exceptions. The importance of an early start of the serotherapy was demonstrated. About 80 per cent of the patients had serum sickness about ten days after the treatment, and in two cases this contributed to the fatal outcome. There were only two deaths in the remaining twenty-two cases, both in cases considered hopeless at the start of treatment. Complications were rare. The author concludes that treatment with type specific serum is a definite therapeutic advance, especially if the serum production is improved so that the grave serum conditions can be avoided; till then, extreme care is called for in treatment with serum of type III.

Auscultation of Cranium.—Dalsgaard-Nielsen says that sounds within the cranial blood vessels demonstrable on auscultation should always suggest a possible vascular tumor but cannot be regarded as pathognomonic, as illustrated in the last two of his six cases, in which the cause of the sound was hydrocephalus and hypertonia, in the one case due to a stenotic aqueduct, in the other to a cerebellar tumor. A cause other than vascular tumor must be suspected in those cases in which a sound within a blood vessel is audible on both sides of the cranium and may be affected by compression of both the right and the left carotid in such a way that the sound disappears on the side on which the carotid is compressed.

THE STUDENT SECTION

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Intern Training: Its Organization

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A certain amount of intern training has been the accepted procedure in most hospitals as a recompense, largely, for intern service. The intern usually has accepted such instruction and experience as have happened to come his way. Seldom has intern instruction had coordinated supervision or even organization. Recently, medical educators have become conscious of certain deficiencies in undergraduate instruction and have felt the necessity of rounding out didactic instruction by practical clinical training, in the endeavor to endow the prospective physician with some practical application of the theoretical achievements of medical school. Mastery of any practical science like medicine is evidenced largely in the ability to conduct skilfully those various technics and procedures which make it applicable, and the degree of this mastery only too often determines the difference between success and failure in practice. The recent graduate is supposed to have, and probably does have, considerable theoretical knowledge regarding medical procedures and their underlying scientific principles; he often, however, has little conception of their practical application. While a student may acquire scientific concepts through lectures and reading, no amount of such study will endow him with a mastery of the art of their application. These various skills which are so essential to medical practice are, or should be, obtained largely by observation and carefully supervised application, made possible during an internship and residency. The intern should realize that his internship may be his only opportunity to develop a skilful mastery of those various technics and procedures which constitute the art of medicine.

Staff members should appreciate the importance of intern training, not solely because of the assumed obligation in accepting intern ser-

vice, but because much of the efficiency of a service depends on the skill exercised by the intern in the execution of various necessary routine procedures. However well a service may be organized, its efficiency depends largely on those less conspicuous activities which ordinarily are considered as resident and intern duties. The attitude of a service chief toward the intern too often has been the relation of master and servant, while it should be that of master and pupil. The efficiency of intern service rests largely on the intern's conviction that he is doing important and necessary work which is duly appreciated, and that he is really being compensated for this service in practical training.

Very few interns are able to appreciate the relative importance of the various procedures which they observe in their hospital work. They often are impressed with spectacular surgical procedures, or perhaps even with the personality of some members of the staff, and may devote their time largely in specialized subjects, to the exclusion of fundamental procedures which later will be required in practice, and on the acquirement of which their medical careers greatly depend; thus, through lack of organized teaching, an internship may be practically wasted. Interns often value a surgical service solely on the number of operations they are allowed to do, little realizing that the actual mechanics of most surgical procedures might readily be executed by an artisan totally untrained in those fundamental principles which determine why and when a given surgical procedure is to be instituted. If this lack of comprehension of relative values existed in medical practice, as it so often does in surgery, the intern might, on a similar basis, value his medical internship on the number of prescriptions he has been allowed to compound.

ORGANIZED GRADUATE TRAINING FOR INTERNS

In instituting graduate instruction arranged for intern training, certain objectives should be kept in mind:

1. In a mixed, or rotating, type of internship the intern should be expected to master the art of certain fundamental technics and procedures as they pertain particularly to each service. The chief of service, with the staff, should therefore outline those fundamentals which an intern should master while on that service. These may be called minimal essentials.

2. In order that the intern's activities be properly supervised and checked, an intern instructor is appointed and assumes the responsibility of the administration of intern instruction in each service.

3. While in any given service the intern, under supervision, will naturally be expected to master certain technics and clinical procedures. The chief of the service, however, should be assured that the intern obtains a comprehensive view of the whole case picture and appreciates the relative value of the various procedures used as they apply to examination, diagnosis and therapy, and, to this end (at least on all staff cases), a summary sheet is filled out by the intern showing positive clinical observations, the pathologic condition (suspected or proved), the therapy instituted and the results. At the completion of each service the intern will submit to the chief of that service a certain number of concise case summaries, each giving an intelligent perspective of a certain assigned case.

4. It is of utmost importance in all teaching to correlate the relationship between disease and symptoms and endeavor to determine the cause of a given disease and the influence of therapy on that disease. In these considerations, our limitations will be so forcibly emphasized that the intern and junior members of the staff will constantly have the stimulation of critical clinical analysis, leading to the development of the scientific spirit. This is termed the consideration of living pathologic conditions.

The foregoing procedure devised for the training of interns places a definite teaching responsibility on the chief of each service. It tends to assure the mastery of at least fundamental technics and procedures. It places responsibility on a definite member of each staff, who is accountable to the chief, for intern instruction. It endeavors to give the intern a comprehensive view of an entire case, tending to develop a conception of the relative values of the different diagnostic and therapeutic procedures. It furthermore insures a consideration of basic sciences in the determination of the influence of a given pathologic condition on normal physiologic reactions in the production of symptoms and tends to stimulate interest in investigation toward determining the cause and effect of a given pathologic condition.

OUTLINE OF MINIMAL ESSENTIALS

In order that the intern may be assured of mastering the basic principles and important fundamental procedures and technics of each

service, a list of minimal essentials should include at least the following:

1. Demonstration of ability to obtain a pertinent and comprehensive case history.

2. Demonstration of ability to make a competent physical examination.

3. Acquirement of competence in special technical procedures (enumerated) and evidence of a comprehension of their use and value.

4. Actual observation and treatment of certain special clinical entities (as outlined).

5. Ability to make a reasonable diagnosis, institute and conduct rational therapy (write prescriptions, apply splints, perform venipuncture, and so on).

6. Attendance at all postmortems, staff rounds, clinical conferences and prescribed clinics.

7. Submission of required summary histories.

A list of minimal essentials is given to the intern as he is assigned to each service. At the completion of each service the intern instructor sends to the intern committee a copy of the list of minimal essentials of that service, having initialed those subjects which a given intern has mastered, with such criticisms or recommendations as he may wish to make.

INTERN INSTRUCTOR

In the organization of intern training in any department, the appointment of an intern instructor is primarily directed toward the administration of intern instruction in that service. When an intern reports to a service for duty, he reports to the resident and intern instructor, is introduced to the chief and staff personnel, and is instructed in service routine and his special duties. The importance of this formal introduction to the service is obvious. The intern instructor's duties are to observe carefully the intern's work, be his confidant, see that he is assigned to various members of the staff for special training when such is necessary, and keep a record of his achievements so far as the mastery of minimal essentials is concerned. The intern instructor may at first feel that he is being shouldered with a lot of responsibility and nonclinical duties which consume considerable time, perhaps more than he can afford to give. This need not be the case, for, after intern instruction has once been organized, it soon develops into a habit procedure which tends to increase the efficiency of the service, in that the well instructed intern greatly promotes the smooth running of a service and eventually saves more time by enhancing efficiency than is given in actual instruction.

In the appointment of the intern instructor, the chief of the service should exercise judgment in selecting one who is thoroughly competent to give intern instruction, has the required personality, is interested in teaching, and will

devote the time and energy required. The intern instructor will constantly keep in mind, in his supervision of the intern's instruction, that no endeavor is being made to make a specialist of the intern, but he should assure himself that the intern is really mastering those various arts of the service which would be expected of a well trained general practitioner who will be capable of appreciating his possibilities and his limitations in any special field.

SUMMARY SHEET

The average hospital chart is usually a rather cumbersome affair filled with many routine details. For an intern to obtain a comprehensive view of a given case from beginning to end, a summary sheet is advisable. The development of this summary should be progressive with the case, a brief outline of the essential clinical observations leading to a given diagnosis, the indications for the specific therapy employed, the result of this therapy, and the pathologic conclusions. The summary sheet should be used with each staff case so that the attending physician or intern may obtain a comprehensive summary of the case to date by examining a single sheet of the history (referring to the chart proper for details). In making rounds, in the operating room, and in clinical conferences, those specifically recorded facts of the summary sheet are readily available and serve to give a perspective which cannot be obtained in any other manner. The summary sheet compiled by the intern serves the chief of the service and the attending physicians particularly well in estimating the intern's ability to comprehend essential and important details in a given case. While an intern is on each service, he should be required to hand to the chief copies of the summary sheets of a certain number of specified cases which he has personally attended.

CONSIDERATION OF LIVING PATHOLOGIC CONDITIONS

Too often, the pathologic material obtained from autopsies and operating room has been considered as material for the pathologic museum or has simply served to affirm, or disprove, a given diagnosis. Hence, from a standpoint of instruction, we have termed our clinical pathology as "living pathology," in contradistinction to its purely laboratory consideration, endeavoring to emphasize the effect of a living and developing pathologic condition within the organism as a disturbing factor in normal physiologic functions and to consider symptoms as abnormal physiologic reactions.

Instead of simply recognizing symptom complexes and clinical signs, one should interpret them in relation to the disturbance caused by a definite pathologic entity, endeavoring always to stimulate a pathologic consciousness, by asking the question "Why did this pathologic condition produce certain symptomatic effects and what caused the original development of the pathologic condition?" A consideration of pathology in this way directs constant attention to basic sciences on which the whole structure of medicine rests.

GENERAL CONSIDERATIONS

Certain requirements are obvious in intern training, such as library facilities, opportunity for reading, proper allotment of time and service assignments, defining of responsibilities, and limitation of procedures, which involve organization in preparation for satisfactory intern service and instruction. The general administration, as well as the staff, of an institution should appreciate the obligation of intern instruction and its value in promoting efficiency in the various services. The four principles introduced herein as a basis for organizing intern instruction were developed in the effort to assure the intern and resident a more complete mastery of those basic principles and artful technics which underlie the practical application of medical knowledge.

These principles were adopted in the organization of intern and resident training of the Flower-Fifth Avenue Hospital, connected with the New York Medical College, New York City.

Overdoses of Technological Training

The medical student and the doctor, too, are in danger of overdoses of technological training and becoming surfeited by undiluted medicine. These studies might profitably be sweetened by the introduction of studies which broaden the views from the narrow picture of disease to the larger scenes of all society. The quality of the doctors would be improved by adding social thinking to their training; the physician might acquire a special medical culture which would impress him with a new conception of medicine as an art and give him a greater concern for the doctor's relationship to humanity. European universities have carried this branch of teaching further than we have. As far back as 425 B. C., Hippocrates wrote a book entitled "Ancient Medicine" in which he discussed doctors and medicine of former times. He said that a physician must know what physicians before him have known; if he did not, he would deceive himself and others. Medical history acquires its best value only as it is converted into medical sociology. This is the atmosphere in which good physicians are bred. Knowledge, because of its commercial uses, is apt to be given a greater value than reasoning, but education is, after all, best concerned with the emphasis on thinking.—Black, B. W.: *Community Aspects of Medicine*, J. A. Am. M. Coll. 13:19 (Jan.) 1938.

Comments and Reviews

ON ENTERING MEDICINE

Many of you, now, are at the threshold of the goal which you have been seeking for many years. The thought may come to some that now that they have reached this pinnacle, the only requisite is barely to satisfy the minimum standards in order to achieve the final award of the doctorate in medicine. An aim of this stature is not adequate. The study and the practice of medicine form one of the most highly specialized professions, with standards of attainment and ethics unequalled in any other profession. The attainment of these standards by those who have gone on before us has not been simple but an unselfish task of grand labors. Thus it behooves us to emulate these pioneers and carry our profession forward. This is, also, an unstinting task, one in which only intelligent, far-seeing planning and accomplishment will promise success.

The technical aspect of medicine increases year by year to the student's consternation, but this is one of the reasons that you have been chosen so carefully. You have, however, the advantage of highly trained, sympathetic instructors to guide you along the path of the science. The art of medicine will be revealed to you in your clinical experiences, but your grasp in this field is a personal problem. Your ability to handle yourself is of supreme importance in the practice of medicine and that has been a major factor in choosing you, a member of the freshman class.

Remember as you consider your lot that medical practice has a long history of leadership and always has been an important influence in the shaping of civilization. This is even more true today than ever before. Constantly look around you, delve, and discover the problems of medicine. You have a glorious heritage. Do not confine yourself entirely to the purely technical aspects. Widen your horizon, broaden the base of your cultural background so that our profession may continue to lead society.

Your entrance into the study of medicine is the beginning of a responsibility and not an end of safe security or intellectual aristocracy. The horizon of medicine is boundless and our knowledge is paltry, in spite of the tremendous amount of truths that have been accumulated and will be passed on to you for mastery. Thus, your course must be broad and unswerving, never losing the concept of the technical and social problems of the profession of medicine in society.

To be a good doctor, one must above all be a gentleman. Within our own buildings, mis-

conduct is laid directly at our door; in the hospitals it is laid first at the door of the medical school. That we are allowed to be present in the wards of the hospitals is a distinct honor and privilege. That privilege must be treated with care lest our welcome be spoiled. The student must be considerate of those about him, particularly patients with whom he comes in contact.

SCHICK REACTIONS IN MEDICAL STUDENTS

During the seven years ending with 1936, each sophomore student at St. Louis University School of Medicine was Schick tested. The majority of the 816 students were between 22 and 27 years of age. Pulley and Fleisher,¹ in making a special study of this group, learned that 72.2 per cent of the sophomores had no history of diphtheria or of immunization; 11.7 per cent gave a history of diphtheria; 10.5 per cent reported active immunization with no history of diphtheria, while 5.4 per cent had been passively immunized. The writers divided the total group of students into subgroups according to their previous place of residence. There were four subgroups including (1) those who resided continuously in a larger community, (2) those who resided continuously in a smaller community, (3) those who were born in a larger and later moved to a smaller community and (4) those who were born in a smaller and later moved to a larger community. A city of less than 50,000 was classed as small. When the data were tabulated, it was found that the percentage of negative Schick reactions decreased in students passing from residence in larger communities to residence in smaller communities.

There was a sharp drop in Schick negative reactions they said in students who resided for some part of their lives in a larger community. This material suggests that even among those exposed to active immunization the likelihood of developing a negative Schick reaction is greater with continuous residence in the larger communities. The Schick negative students were slightly more common among those who had lived permanently in larger communities than among those who had spent a portion of their lives in small communities, and considerably more frequent among those who resided constantly in smaller communities. The authors caution against drawing definite conclusions from these relatively small groups. However, they suggest, as others have, the relative importance of residence in a larger community in the development of natural immunity to diphtheria.

The Schick negative students comprised 64.5 per cent of the entire group, which is lower than might be expected; somewhat low also was the 76.4 per cent of Schick negative tests among those who had been exposed to active immunization.

The authors consider that the most striking tendency which appeared in this study was a gradual diminution during the seven year period of Schick negative reactions among those who gave no history of exposure to active immunity. The factor of residence was not considered responsible for this change. It is more likely due, they say, to lack of exposure to subclinical contact with diphtheria bacilli. This raises an interesting question in relation to the control of diphtheria, since it is assumed that the development of immunity in persons nonactively immunized is related to contact with the causative agent. If active immunization tends to reduce the opportunities for contact with diphtheria bacilli, then those persons who have not been actively immunized must be especially guarded, or the immunization campaigns must be carried on with vigor in order to cover as nearly 100 per cent of persons as possible.

THE MEDICAL CURRICULUM AND PRESENT-DAY NEEDS

Sir Walter Langdon-Brown has been a member of three committees, each one designed to improve and lighten the medical curriculum, but the results of the lengthy deliberations, he says, were not impressive. Every one on the committee agreed that the curriculum ought to be lightened, but each thought that the other man's subject could be cut down while more attention should be given to his own. The anatomists were steadfast, unmovable, always abounding in the faith that dissection of the whole body is necessary unto salvation. Many nonanatomists do not think so. When men say that after demonstrating anatomy for ten years or so they rapidly forget the finer details and remember only what is of practical importance to their surgery, then how much anatomic detail can one expect the average student to remember? In his time, the author said, they were taught almost as much error as truth so far as the viscera were concerned. Today the student sees on the screen the stomach as it is in life and activity; he learns its variability within the limits of normal. He sees the skeleton living and moving on the fluorescent screen. But is it fair to expect the student to carry the whole weight of the old anatomy in addition to the new?

* Abstract of a paper by Sir Walter Langdon-Brown, Emeritus Professor of Physics, University of Cambridge, England, published in the Educational Number of the British Medical Journal, Sept. 3, 1938.

Physiology has become almost as abstract as physics, and a survey of examination results suggests that in some schools the teaching of it has departed from the lines suitable for the training of those designed to become doctors and not whole-time physiologists. If this is so, it is to be regretted, for there is no sounder foundation for medicine than physiology.

Materia medica has been cut down almost to the vanishing point in most curriculums, and rightly so. Now that the old type of apothecary has disappeared, doctors do not handle the raw material from which medicines are made, and the time formerly occupied in learning about them can be more profitably employed. As to the teaching of pharmacology, this has largely come under the aegis of the physiologist, who has in turn handed over histology to the anatomist. The author is strongly in favor of the examination in this subject being conducted by pharmacologists and clinicians working in pairs. In this way its practical therapeutic aspect is kept to the fore.

OBSERVATIONS IN THE WARDS

It is alleged that the student today relies too much on what he is told rather than on what he can observe for himself. For this the examination system is somewhat to blame. Nothing can take the place of living in the wards as much as possible and observing closely the progress of actual cases.

It is a special advantage of our English plan of clinical clerkship that the student is taught to regard a certain number of the ward inmates as his patients—he is their doctor; the personal individual relation is encouraged from the very beginning, and it is the best introduction to general practice. "I used to make it a point to urge on all my students the prime importance of taking a full history. As time goes on, I have found myself taking more and more time over the history compared with the time occupied by the physical examination." The history tells so much about patients, their general outlook and temperament, and prepares them for the kind of examination specially called for. Remember the enormous difference in the effect on the patient that can be produced by your attitude toward him. Patients are in a state of fear—whether obvious or concealed. They are watching you closely and are much more ready to accept an unfavorable than a favorable suggestion. Keep a straight face when the patient tells you his interpretation of his symptoms, however preposterous it may be. The patient's statements, though demonstrably false, tell a lot about him.

THE PSYCHOLOGIC ASPECTS OF DISEASE

It is highly important that the student be made familiar with the psychologic aspects of patients in hospital, whether they are under

treatment for organic disease or for functional nervous disorders or are admitted merely for observation. With this object, a series of demonstrations should be held at least once a fortnight throughout the student's period of inpatient clerking and inpatient dressing. In every ward there are patients suitable for demonstrations of this kind, but a considerable amount of time is required in some instances for their preliminary study by a psychotherapist before they can be used for the purposes of teaching. In some schools such demonstrations have met with great success. The physician or surgeon in charge of the ward may undertake them or may hand over that duty to a colleague who is attached to the hospital for the purpose of teaching medical psychology.

In the final qualifying examination adequate knowledge of the psychologic aspects of ill health should be expected from the candidates. My experience as a teacher has shown that the pressure to teach the neuroses is coming from below—the students are eager for it, and if they don't get it from one man or in one school they will go elsewhere. In the future no school will be able to maintain its prestige if it persists in neglecting its opportunities in this direction. In this way, a man going into practice would not have the humiliating experience of finding himself confronted with conditions that he had never encountered in textbooks. Having allowed for or excluded organic factors, he would know how to look for the psychic causes at work. Above all, we must not overwhelm the student with a mass of facts at the expense of developing his powers of observation and deduction. With those powers, he will be able to go on educating himself.

THE EXAMINATIONS

The plan instituted in the National University of Ireland by Prof. Henry Moore at Dublin is the best I have met with. It necessitates three pairs of examiners. The candidates have an hour to examine and write up their first case; they are then put on to a second case, which they go over in the presence of two examiners, pass on to a "spot" case with two more, and are finally cross-questioned on their first by the examiners who have had an opportunity of reading the scripts. The examiners deal with the same cases; it is the candidates who change over. As no candidate should pass who fails to obtain half marks in the clinical examination, it is wise that such a decision should depend on the judgment of more than one pair of examiners. Most examiners of experience are confident that they can judge a candidate's capacity better by oral than by written examination. This is true if the candidate remains in a normal state of mind; unfortunately some of them seem to become disoriented and aphasic under

the ordeal. Every effort should be made not to keep candidates locked up and waiting for a long time; for fear is infectious under such conditions.

THE CANDIDATES

The examiners have all been candidates themselves and know both the difficulties experienced and the devices adopted. Do not imagine they are out to trap you. Map out your time for the different questions in the papers. It is not easy to gain many extra marks by a specially long answer, while to omit a whole question for lack of time seriously reduces your total. It is easy, on the other hand, to get from 25 to 30 per cent of the marks by giving a synopsis of an answer if you have not allowed yourself time to answer it fully. Don't give rare causes first; it only proves you lack a sense of proportion. If at the oral you do not know the answer to a question, say so—do not waste time which should be devoted to gaining more marks by glaring helplessly at the examiner. You will get more credit for routine examination of the patient and good observation than for a lucky shot at the diagnosis. Put clinical points first. If asked what is the first thing to do when called to see a case of jaundice, do not reply, "I would do a van den Bergh," or that the first thing you would do for hematemesis is to give a barium meal. You would do nothing of the sort. The attitude of clinical teachers may do something to contribute to developing this absurd state of mind. The student is influenced more by what he sees his teacher do than by what is said, and he is quick to notice that the newer methods interest the teacher most.

"Let me welcome recruits for the study of the most fascinating, if one of the most exasperating, professions. Its combination of scientific and human interest will provide the satisfying feeling that a life spent in its pursuit has not been lived in vain."

WOMEN IN MEDICINE

"The most important requisite for any one wishing to study medicine is the possession of a clear objective, a desire for the work so definite that all other things fade in importance, for medicine is a jealous mistress. Presupposing determination and a general aptitude for the work, the next most important factors are health, personality and money." Thus the *International Altruist* tells in a recent issue what the prospective medical student may expect and must have.

Women are especially well suited to practice medicine if they are intelligent enough to practice sanely and scientifically, instead of emotionally. Women, scientifically trained, emotionally stable, can be and are among our best obstetricians. Not strength but wisdom and good judgment are needed.

Women in medicine should not try to overcome their feminine tendencies, the article

declares; as women they have special contributions to make. They should prize their intuitive powers and should remain and work as women. Being oneself leads to more success than imitating others.

Prof. Arthur Curtis of the University of Michigan says that the average educational standard of women entering medical school is higher than that of men. A smaller percentage of women who enter medical school fail than men. However, there are not as many women studying medicine now as there were twenty-five years ago. This is probably due to the other fields that have been opened up to them.

Although not many women have entered the field of surgery, women do make good surgeons and are increasing in number as opportunities for postgraduate study are available to them in the many specialized branches.

THE BRITISH EDUCATIONAL NUMBER

The British Medical Association publishes annually an educational number of the *British Medical Journal* in order to inform students and their parents of what must be done to become a registered medical practitioner and to help those who desire to know what a medical career has to offer. In a general article entitled "The Profession of Medicine," the cost of medical education, the choice of a career, general practice, consulting practice and professional organization are considered. There is an account of the training required of students, the places where it can be obtained and the organizations that confer degrees or diplomas entitling successful candidates to become legally qualified medical practitioners.

It is advised generally that any one who thinks of entering the profession should be prepared for an outlay of at least 1,500 pounds, since their professional education must continue for five years. Something more than two thirds of this total would probably be spent on maintenance, and the rest in tuition, fees for examinations and admission to degrees or diplomas. For those who live in rooms away from home, 120 pounds per annum for board, lodging and the like is considered a minimum figure. There are, however, many ways for students to reduce the expense at most of the medical schools in the way of scholarships and money prizes offered. The General Medical Council has issued for the guidance of students a memorandum which gives information about the comparative cost of study and examinations at the various medical schools.

THE NUMBER OF DOCTORS

The Medical Register is the official list of legally qualified medical practitioners kept by the General Medical Council. The total number on this list Dec. 31, 1937, was 60,163, of whom 2,214 had been added in the last year. The

number of practitioners was 20,350 more than it was thirty years ago. The population of the British Isles has not increased at anything like that rate, and the ratio of doctors to inhabitants is much higher now than it was formerly. It is safe to say, the *British Medical Journal* adds, that at present there are quite enough doctors to satisfy present demands; on the other hand, the regius professor of medicine at Oxford has publicly expressed the opinion that the profession is far from being overcrowded. His opinion apparently is based on the belief that the work of doctors in the future will be somewhat different from what it has been in the past and will be that of preserving health and preventing disease. Some 10 per cent of the total number of registered practitioners in the British Isles today are women. According to returns published by the University Grants Committee, women constituted 16.1 per cent of the total full time students of medicine and dentistry in England, Scotland and Wales in the academic year 1936-1937.

The British Medical Association has stated as an axiom that medical service of the community must be based on the provision for every individual of a general practitioner or family doctor. Some twenty-five years ago medical practice in the British Isles saw a radical change in the institution of a national system of compulsory health insurance. The insurance system, the *British Medical Journal* says, has induced a better class of men to enter the profession, by raising the standard of living among doctors. The Insurance Acts provide domiciliary medical attendance for about nineteen million persons, and more than 19,000 doctors undertake the medical care of this vast part of the community. By placing their names on the panel list, these practitioners agree to comply with the terms of the service set out in the Medical Benefit Regulations and other relevant provisions.

CONSULTING PRACTICE

Success as a consultant or specialist is hard to achieve in the British Isles, except by the aid of appointments to hospitals, particularly those with medical schools, and the time to wait for appointment to these much sought after positions usually is long. In the larger industrial towns of the North of England, there are many "general practitioner specialists" who combine panel practice with surgical or other special work in well equipped hospitals which admit patients in different categories according to their means. In securing election to the visiting staff of the large hospital, additional degrees and diplomas are important factors and a considerable number of those who have graduated as M.B. from a medical school, including many general practitioners, proceed later to attain the M.D. There are in England three medical cor-

porations which grant licenses to practice, the Royal College of Physicians of London, the Royal College of Surgeons of England, and the Society of Apothecaries of London.

THE GENERAL MEDICAL COUNCIL

The conditions with which those who wish to enter the medical profession must comply are regulated by the General Medical Council, which is a statutory body established by law in 1858. The duties of the council are (1) to keep the Medical Register; (2) to see that no person is listed in the Register as qualified unless he has had an adequate education and to remove from the Register the names of qualified persons who are no longer entitled to public confidence, and (3) to provide for the publication of the British Pharmacopeia. It is the entry of a name on the Medical Register and not the possession of a diploma or degree that constitutes a person as a legally qualified practitioner of medicine. The General Medical Council has thirty-nine members, eighteen of whom are appointed by the universities of the United Kingdom having medical faculties; nine by the medical corporations, such as the Royal College of Physicians and Surgeons; five by His Majesty in Council, and seven are elected by members of the profession as a whole; to these are added three dentists who are members of the Dental Board. Although twenty-three of the thirty-nine members may be laymen, only two laymen have ever been appointed, and both of these were members of His Majesty's Privy Council.

There are eleven universities in England and Wales, all having fully developed medical faculties; four universities in Scotland (St. Andrews, Glasgow, Aberdeen and Edinburgh), and three universities in Ireland (the University of Dublin, the National University of Ireland and Queen's University of Belfast), each with a medical faculty. There is given a brief account of all the universities.

GRADUATE STUDY

The facilities for graduate study include the British Postgraduate Medical School, which is a part of the University of London and is associated with the 534 bed Hammersmith Hospital. The school provides refresher courses of an intensive character for general practitioners, but the most important part of the tuition, it is said, is the instruction provided for medical graduates from all parts of the world who desire to extend their knowledge in medicine or surgery, or midwifery, and for students of pathology who desire to do advanced work. Among other facilities for graduate work are the North East London Postgraduate College, the Radium Institute and Mount Vernon Hospital, the West End Hospital for Nervous Diseases, the Fellowship of Medicine and Postgraduate Medical Association,

and the facilities for graduate study in Manchester, Bristol, New Castle, Cardiff, Edinburgh and Glasgow.

An important development in graduate study facilities took place during the last year, whereby an arrangement was made with the ministry of health to afford graduate facilities for some insurance practitioners, including for 1938 about 800 places in England, 100 in Wales, and 250 in Scotland. The conditions to obtain a grant for a practitioner to attend such a course are: (1) that he has not less than 300, or in rural practice 150, insured persons on his list, (2) that five years has elapsed since the date of his first registrable qualification, (3) that no grant will be made to a practitioner more than once in five years. A grant for the course covers (1) the fee but not exceeding 5 guineas unless specially authorized, (2) traveling expenses, (3) subsistence not exceeding £5 a week if the practitioner sleeps away from home, or £1 in other cases, (4) not exceeding 8 guineas a week where necessary, for a whole-time locum tenent. During the first year of this arrangement there were about three times as many applicants as there were places available.

Other sections in the educational number intended to help students comprise discussions of the Royal Navy Medical Service, the Royal Army Corps, the Medical Branch of the Royal Air Force, the Indian Medical Service, the Prison Medical Service, the Colonial Medical Service, the Sudan Medical Service, facilities for the study of tropical medicine and psychological medicine, and finally a brief description of the British Medical Association, with a picture of its building at Tavistock Square, London, W. C. 1, England.

APPENDICITIS IN COLLEGE STUDENTS

Schmidt and Joachim¹ report a study of appendicitis as observed in the Student Health Department at the University of Wisconsin from 1926 to 1937, including 615 admissions to the University Infirmary for appendicitis. The patients were healthy, intelligent young adults who came to the infirmary within a few hours after the onset of their symptoms. Very few of them had resorted to self medication. There is an advantage in treating a select group of young adults under such desirable conditions, and that was responsible at least in part for the mortality rate, which was 0 in this group of students.

The good results have been reported in the management of appendicitis by student health departments elsewhere. The average age of these patients was 20 years, and 75 per cent of them were seen at the infirmary before their

1. Schmidt, E. R., and Joachim, F. G.: The Student Health Problem of Appendicitis, *Journal-Lancet* 58: 329 (July) 1938.

symptoms were twenty-four hours old. The advantage of early hospitalization is again shown in their unusual freedom from complications. The appendix was ruptured in only twelve cases. Half of the patients with a perforated appendix were operated on and the other half were treated conservatively. Peritonitis was localized in all the cases but one in which the appendix was perforated, and that case responded well to conservative treatment.

Schmidt and his associates treated about an equal number of patients with appendicitis at the State of Wisconsin General Hospital proper, which is adjacent to and in fact connected with the Student Infirmary. The personnel who cared for these two groups of appendicitis patients was identical. Comparison of the two groups shows that whereas the students' ages ranged from 18 to 21 years, one third of the group of patients from the State of Wisconsin General

Hospital were either under 10 years of age or over 30. Only 45 per cent of the patients in the State of Wisconsin General Hospital were admitted on the first day of illness, as contrasted to 75 per cent in the Student Infirmary group. Furthermore, 20 per cent of the hospital patients had taken a cathartic prior to admission. The appendix had ruptured in 19 per cent of the hospital patients as contrasted with only 2 per cent in the student group. The gross mortality of the State of Wisconsin General Hospital group was 5.68 per cent and that of the student group, 0.

This comparative study seems to show that success in the treatment of appendicitis depends on the age of the patient, the duration of the illness and the matter of self medication. The conditions attending the treatment of acute appendicitis in a student health practice are optimal.

Medical College News

Medical schools, hospitals and individuals will confer a favor by sending to these headquarters original contributions, reviews and news items to be considered for publication in the Student Section.

Vacancies for Interns

There are now vacancies for second year medical interns in the United States Public Health Service, particularly at government hospitals located at Lexington, Ky., and Fort Worth, Texas, and some of the federal penal and correctional institutions. Detailed information may be obtained by writing to the Surgeon General, United States Public Health Service, Washington, D. C., or to Dr. Fletcher C. Stewart, medical officer in charge, U. S. Marine Hospital, Evansville, Ind.

National Research Council Fellowships Available

The National Research Council announces that fellowships in the medical sciences will be available for the year beginning July 1, 1939, open to citizens of the United States and Canada with M.D. or Ph.D. degrees. They are intended for recent graduates and not for persons already professionally established. Appointments will be about March 1, 1939, and applications must be filed on or before January 1. For further particulars concerning these fellowships, address the secretary of the Medical Fellowship Board, National Research Council, 2101 Constitution Avenue, Washington, D. C.

Ward Rounds for Students

In response to a request from the University of Rochester School of Medicine, the Medical Board of the Rochester General Hospital recommended that the hospital cooperate with the university by permitting small groups of students to make rounds in the wards with the visiting staff. On September 27 six members of the third year class in surgery, and on October 1 nine members of the third year class in obstetrics made ward rounds. At the meeting of the medical board of the hospital September 16 Dr. James K. Quigley was elected chairman, Dr. Edward T. Wentworth vice chairman and Dr. Leslie R. Lingeman secretary-treasurer.

Gift for Research in Tuberculosis

The trustees of the Albany Medical College announced the receipt of a \$100,000 trust fund for research in tuberculosis and pharmacology from the estate of the late Dr. Howard Van Rensselaer, professor of therapeutics at the college for many years. Under the terms of the will, Dr. Van Rensselaer, who died in March 1925, left half of his estate, after payment of certain legacies, in trust to his sister-in-law Mrs. William Bayard Van Rensselaer. On her death the trust fund was left to Union University, the income to be expended under the direction of the Albany Medical College for research in tuberculosis and pharmacology.

Faculty Changes at Jefferson Medical College

At the formal opening of the Jefferson Medical College, Philadelphia, September 20, the following appointments to the faculty were announced:

Dr. Bernard J. Alpers, assistant professor of neurology, at the graduate school of medicine, University of Pennsylvania, has been appointed to the chair of neurology.

Dr. Henry K. Mohler, the new dean, succeeding the late Dean Ross V. Patterson, will also be the Sutherland M. Prevost professor of therapeutics.

Dr. James Torrance Rugh has consented to amend his resignation so that it will take effect only when a suitable successor can be obtained to fill the James Edwards chair of orthopedic surgery.

This year's freshman class of 143 students was selected from about 650 applicants. Thirty-one members of the new class of students are either the sons or other near relatives of physicians.

Arthritis Research Unit at Michigan

The recently established Rackham Arthritis Research Unit at the University of Michigan already has under way a program of investigation. At present the studies are confined to cases of active rheumatoid arthritis, gonorrheal arthritis, psoriatic arthritis and gout, the clinical studies being on patients referred from other university clinics, and include a complete physical

examination, a thorough study of the patient's history, laboratory studies and carefully controlled treatment. Biochemical investigations which have a direct clinical application and bacteriologic and immunologic studies are being made. The staff of the Rackham Arthritis Research Unit at present comprises Drs. Richard H. Freyberg and Charley J. Smyth; biochemist, W. D. Block; bacteriologist, W. S. Preston, and Miss M. E. Bishop, laboratory assistant. It is expected that other laboratory assistants and a nurse will be added to the staff in the near future.

Michigan Personals

Dr. Ferdinand Gaensbauer has returned to Ann Arbor and is again serving as instructor in the department of obstetrics and gynecology at the University of Michigan Medical School.—Dr. Ward W. Woods, assistant resident in surgery at the University Hospital in Ann Arbor, has accepted a fellowship in neurosurgery at the National Hospital for the Paralyzed and Epileptic, Queen Square, London, England.—Dr. Herbert C. Maier, instructor in thoracic surgery, University Hospital, Ann Arbor, has returned to New York City, where he will be resident in thoracic surgery at Bellevue Hospital.

Tufts Awards Commonwealth Fund Scholarships

The Tufts College Medical School, Boston, has awarded the Commonwealth Fund Scholarships for the class of 1942 to Willard H. Boynton of Groveland, Mass.; Alfred G. Chandler of Candia, N. H.; John B. Madigan of Houlton, Me., and John R. Williams of Fair Haven, Vt. The scholarships are \$1,000 a year for four years, and the recipients must agree to practice medicine in a rural community of Massachusetts for three years. They must also complete a rotating type of internship in approved hospitals for a period of two years before beginning actual practice.

New Faculty Members at Oklahoma

Donald B. McMullen, D.Sc., professor and head of the department of biology, Monmouth (Ill.) College, has been appointed professor of bacteriology at the University of Oklahoma School of Medicine, Oklahoma City. Rudolph F. Nunnemacher, A.M., Harvard University, Cambridge, has been appointed instructor in histology and the following have been made assistants in medicine: Drs. Allen G. Gibbs, Vern H. Musick and Ralph A. Smith. Dr. Hubert E. Doudna has been appointed lecturer in anesthesia and head of the department of anesthesia in the University and Crippled Children's hospitals.

Award of Foundation Prize

Dr. Wallace E. Herrell of the Mayo Foundation, Rochester, Minn., has received the first award of the Foundation Prize of the Association of Obstetricians, Gynecologists and Abdominal Surgeons. His paper, entitled "Studies of the Endometrium in Association with the Normal Menstrual Cycle, with Ovarian Dysfunctions and with Cancer of the Uterus," was presented September 24 at the fifty-first meeting of the society at White Sulphur Springs, W. Va.

Tennessee Personal

Dr. Henry Packer, director of the Carter County health department, Elizabethton, for several months, has been appointed associate professor of preventive medicine at the University of Tennessee College of Medicine, Memphis, newspapers report. Dr. Packer

was graduated from McGill University Faculty of Medicine, Montreal, Canada, in 1933 and later took the degree of doctor of public health at Yale University, New Haven, Conn. He was formerly assistant director of the Gibson County health unit.

Faculty Changes at Woman's College

Dr. Lida Stewart Cogill has retired as professor of obstetrics at the Woman's Medical College of Pennsylvania and has been succeeded by Dr. Ann Gray Taylor. Dr. Henry D. Jump, professor of applied therapeutics, has also retired and Dr. Frieda Baumann has been appointed to succeed him. The following promotions have been announced:

Dr. Ruth N. Miller, associate professor of anatomy.
Dr. Jean Crump, associate professor of pediatrics.
Alice O. Curwen, Ph.D., associate professor of anatomy.
Yersa V. Cole, Ph.D., associate professor of pharmacology.
Dr. Elizabeth S. Waugh, assistant clinical professor of obstetrics.
Ruth E. Miller, Ph.D., assistant professor of bacteriology.
Dr. F. Marian Williams, associate in clinical proctology.
Dr. Laura E. McClure, associate in clinical pediatrics.
Dr. James A. Lehman, associate in clinical surgery.
Dr. Yetta E. Deitch, associate in clinical dermatology.

Dr. Dorothy D. Miller has been appointed instructor in clinical obstetrics; Dr. Carmen C. Thomas, instructor in clinical dermatology, and Vivian Gould Behrmann, M.S., instructor in physiologic chemistry.

At the opening of the 89th year of the Woman's Medical College of Pennsylvania, September 21, the president, Dr. Chevalier Jackson, presided, and the students were addressed by Dr. Earl D. Bond, professor of psychiatry, University of Pennsylvania School of Medicine.

Gifts to New York University

Cash and bequests amounting to more than \$200,000 have recently been made to New York University. Among those to be applied to medical work are the following:

Mr. Bernard Baruch and family, \$1,000 for the Insurance Company, \$1,982; Lederle
Mrs. Cornelius Crane, \$500; other donors
in pneumonia under Dr. Jesse G. M. Bullock.
Felix M. and Frieda Schilt Warburg Foundation, \$5,000 and
sundry donors, \$7,242 for the John Wyckoff Memorial Fellowship
Fund.
Committee for the Study of Suicide, \$8,000 for the study of
suicide under Dr. Karl M. Bowman.
Research Foundation, \$2,000 for research in
cancer under Prof. Robert Chambers.
Phi Delta Epsilon Fraternity, \$1,500 for the John Wyckoff
Lectureship fund.
Winthrop Chemical Company, \$1,500 to establish the Winthrop
Chemical Diagnostic Fund under the direction of Dr. Arthur C.
DeGraff.
Josiah Macy Jr. Foundation, \$1,500 for work in pharmacology
under Dr. George B. Wallace.
Friedman Foundation, \$1,500 for research in urology under
Dr. Meredith F. Campbell.
National Committee on Maternal Health, \$1,185 for the Robert
L. Dickinson Research Fellowship Fund.

South Carolina Personal

Dr. Thomas M. Peery, formerly with the Medical College of the State of South Carolina at Charleston, recently accepted a position in the Department of Pathology of George Washington University School of Medicine, Washington, D. C.

Dr. Whitacre Accepts Post in China

Dr. Frank E. Whitacre, assistant professor of obstetrics and gynecology at the University of Chicago and instructor for the postgraduate program of obstetrics in Tennessee for the past two years, has accepted an appointment with the Rockefeller Foundation to become head of the department of obstetrics and gynecology at Peiping Union Medical College, Peiping, China. Dr. Whitacre will sail for China immediately following the completion of his contract with the Tennessee State Medical Association, which ends December 1.

The Oldest Medical School Building

The college building at the University of Maryland School of Medicine, at Lombard and Greene streets, Baltimore, is said to be the oldest structure in America devoted to medical teaching. According to the Bulletin of the School of Medicine, University of Maryland, in this building was founded the first medical college library in the United States. Here also dissecting was made a compulsory part of the curriculum for the first time in America. The school of medicine at the University of Maryland was chartered in 1808 and ranks fifth in the point of age among the medical colleges in the United States. It was one of the first to provide for adequate clinical instruction by erecting in 1823 its own hospital, and in this hospital intramural residency for the senior student was first established. In 1934 a new university hospital was opened, with a capacity of about 400 beds, of which about 270 are available for teaching. A new building to house most of the preclinical branches will be ready for occupancy at the beginning of the 1939 fall session.

Appointments at Marquette University School of Medicine

The following new appointments have been made to the faculty of Marquette University School of Medicine, Milwaukee:

Dr. Roland S. Cron, clinical professor and director of the department of obstetrics and gynecology.

Dr. Henry O. McMahon, clinical professor and director of the department of pediatrics.

Dr. Albert H. Lahmann, assistant clinical professor of obstetrics and gynecology.

Dr. Raymond A. Hershberg, supervisor of students at the Milwaukee County General Hospital.

Dr. John Kenneth Karr, clinical instructor in medicine.

Dr. Valorus F. Laug, clinical instructor in medicine.

Dr. James P. Conway, clinical instructor in medicine.

Dr. Elwood W. Mason, clinical instructor in medicine.

Dr. Joseph J. Furlong, clinical instructor in medicine.

Dr. John L. Yates, research associate in oncology.

Since the opening of the fall term, two convocations of faculty and students have been held. At the September 26 convocation Dr. Rock Sleyster, Wauwatosa, President-Elect of the American Medical Association and a member of the board of trustees of Marquette University School of Medicine, was chairman, and Dr. Albert E. Rector, Appleton, president of the State Medical Society of Wisconsin, spoke on "The Present and Future Status of Medical Practice." At the October 8 convocation Dr. Herbert M. Evans, Berkeley, director of the Institute of Experimental Biology, University of California, spoke on "Gonadotropic Hormones—A Comparison of Those Found in the Anterior Hypophysis, in the Urine of Pregnant Women, and in the Blood Stream of Pregnant Mares."

Indiana Personals

Dr. Wendell C. Kelly, Indianapolis, assumed his duties as chief of the Bureau of Venereal Disease Control of the Indiana State Board of Health July 1. Dr. Kelly graduated from the Indiana University School of Medicine in 1936.—Robert E. Lyons, Ph.D., has resigned as head of the Indiana University chemistry department after forty-nine years of service. Herman T. Briscoe, Ph.D., a member of the chemistry department faculty since 1922, will succeed Dr. Lyons.

Medical Licensure Limited to Citizens

The West Virginia Public Health Council recently adopted a resolution limiting the license to practice medicine and surgery in the state to native born citizens and those who have acquired full citizenship. Each native born citizen is to submit a birth certificate and each foreign born applicant a photostatic

copy of his naturalization papers. At the same meeting the council adopted a resolution declaring that graduates of unclassified medical schools will not henceforth be considered for licensure either by examination or by reciprocity.

Illinois Personal

Dr. Haskel Maier, formerly an intern in the department of otolaryngology at the University Hospital, Ann Arbor, Mich., has accepted a residency in the Ear, Nose and Throat Department at Michael Reese Hospital, Chicago.

Appointments at the University of Texas

Among the new appointments at the University of Texas School of Medicine announced are Warren C. Woelfel, M.S., instructor in biologic chemistry; Dr. George M. Decherd Jr., formerly at Louisiana State University, to be associate professor in the practice of medicine; Drs. Ernest A. Maxwell and William D. Seybold to be instructors in anatomy; Dr. James O. Chambers to be instructor in pathology.

Grant for Research in Biochemistry at Pittsburgh

The Buhl Foundation grant for research in biochemistry has been renewed for the college year 1938-1939 for studies on vitamin C, tissue respiration and molecular structure in the department of chemistry of the University of Pittsburgh. The following research fellows were appointed under the renewed grant: Max O. Schultze, Ph.D., Wisconsin, animal nutrition and tissue respiration; Rade R. Musulin, Ph.D., Pittsburgh, animal nutrition, and Herbert E. Longenecker, Ph.D., Pennsylvania State College, the molecular structure of fats. Charles Glen King, Ph.D., professor of chemistry, is director of the general project.

Changes in Personnel at Stanford

The following new appointments and other changes in personnel in the department of pharmacology, Stanford University School of Medicine, San Francisco, have been announced:

Dr. Windsor C. Cutting, as assistant professor of therapeutics, full time; formerly fellow of the National Research Council for one year at the Courtauld Institute of Biochemistry, London, and for two years fellow in experimental therapeutics and medicine, Johns Hopkins University School of Medicine, Baltimore.

Dr. Arthur P. Richardson, instructor in pharmacology, as fellow of the National Research Council for one year at the department of pharmacology, Johns Hopkins University School of Medicine, Baltimore.

Walton Van Winkle Jr., assistant in research and instruction, as instructor in pharmacology.

Mrs. Nancy Kidd Kennedy, formerly research assistant in pharmacology, Yale University, and Mr. M. C. Morton (A.B., Stanford) as assistants in research.

Dr. Anthony E. Ambrose, assistant in research, and junior pharmacologist, pharmacology research unit, U. S. Department of Agriculture, as assistant professor of pharmacology, University of Louisville School of Medicine, Louisville.

Dr. Arnold J. Lehman research associate during the summer quarter, 1938, at Stanford, and assistant professor of pharmacology, University of Oklahoma School of Medicine, Oklahoma City, as associate professor of pharmacology, George Washington University School of Medicine, Washington, D. C., beginning the second semester 1939.

Kentucky Personal

Alfred W. Homberger, Ph.D., head of the department of chemistry at the University of Louisville, was given a testimonial dinner sponsored by the Chemistry Club Alumni Association, in recognition of his twenty years service to the university. Dr. Aura J. Miller, professor and head of the department of pathology and serology of the School of Medicine, was master of ceremonies. A silver tray with "H₂O" engraved on it was presented to Dr. Homberger.

Changes at Medical College of Virginia

Faculty promotions at the Medical College of Virginia, Richmond, were recently announced as follows:

Dr. Stuart N. Michaux, professor of gynecology.
Dr. Robert H. Courtney, professor of ophthalmology.
Dr. Robert Finley Gayle Jr., professor of neuropsychiatry.
Dr. Thomas W. Murrell, professor of dermatology and syphilology.
Dr. Lee E. Sutton Jr., professor of pediatrics.
Dr. William D. Suggs, assistant professor of gynecology.

New appointments include that of Dr. Joseph F. Geisinger, Richmond, as professor of clinical urology. Dr. Wyndham B. Blanton resigned last session as professor of the history of medicine and has been made associate professor of medicine. The following were made professors emeritus on their retirement July 1:

Dr. St. George Tucker Grinnan, pediatrics.
Dr. Emory Hill, ophthalmology.
Dr. Edward P. McGavock, dermatology and syphilology.
Dr. Charles R. Robins, gynecology.
Dr. Beverley R. Tucker, neuropsychiatry.

Philadelphia Personal

Dr. Charles J. Miller, chief resident physician at Mount Sinai Hospital, has received the Shmookler Memorial Fellowship and will spend a year at the Graduate Hospital of the University of Pennsylvania working in internal medicine.

The Shoemaker Prize for Senior Students

Dr. Jerome Kotleroff, a graduate of the University of Maryland School of Medicine in June, was awarded the Samuel M. Shoemaker prize for the best essay on "Milk in Relation to Public Health." This annual award for senior students was established as a memorial to the late Mr. Shoemaker, for many years president of the board of regents of the University of Maryland, by Mrs. Shoemaker and Mrs. Bartlett F. Johnston. *Baltimore Health News* says that probably no person was more responsible than Mr. Shoemaker for improvements in the sanitary quality of milk supplies in Maryland during his lifetime.

Louisiana Personal

Dr. Edwin Socola has been appointed clinical professor and Dr. Athol Stewart Kenney assistant professor in the department of pediatrics at the Louisiana State University School of Medicine, New Orleans.

Appointment of Dean in the Philippines

Dr. Bonifacio Mencias, Manila, has been appointed dean of the University of Santo Tomas College of Medicine and Surgery, Manila. Dr. Mencias, who graduated from Santo Tomas in 1915, was president of the Manila Medical Society in 1937.

Dr. MacDonald Heads New Orleans Child Guidance Clinic

Dr. Martha MacDonald, who for three years has been in charge of the Children's Division of the Department of Psychiatry at Michael Reese Hospital, has been appointed director of a new child guidance clinic established in New Orleans. This clinic has been made possible through the contribution of Mr. Samuel Zennurray, president of the United Fruit Company. It will be closely associated with the departments of medicine of Tulane and Louisiana State University and promises to fill a long felt need in New Orleans and to provide leadership to this section of the country. Dr. MacDonald graduated from the University of Pittsburgh School of Medicine in 1924.

Prizes Awarded at Albany Medical College

At the 137th commencement of Albany (N. Y.) Medical College, recently, awards and prizes were made as follows: The John Milton Bigelow Prize was awarded to Dr. Donald Langworthy Burdick; the S. Oakley Vander Pool Prize to Dr. Samuel Stanley Dorrance; the first prize under the Daggett Trust was awarded Dr. Donald Rieh Lyon and the second prize to Dr. Ethel Gladys Cermak. Members of the freshman class who received prizes were Ethel Burack and Irving Cramer, who were awarded the first and second Daggett Anatomical prizes respectively; Mr. Samuel Kantor of the junior class received the Townsend Physiological Prize.

Maryland Personal

Francis Owen Rice, D.Sc., associate professor of chemistry, has resigned from the faculty of the Johns Hopkins University to become professor of chemistry and head of the department of chemistry of the Catholic University of America, Washington, D. C.

Appointments and Promotions at Wayne University

The following appointments have been announced at the Wayne University College of Medicine, Detroit:

Dr. Edgar H. Norris, professor of pathology.
Hans O. Haterius, Ph.D., associate professor of physiology.
Dr. Paul H. Noth, assistant professor of medicine.

Dr. Richard M. Johnson has been promoted from assistant professor of medicine to associate professor of medicine to be in charge of teaching at Eloise Hospital. Dr. Johnson has been appointed medical director of Eloise Hospital.

Fellowships in Psychiatry Awarded

The National Committee for Mental Hygiene announces the following fellowship appointments for one year's training in extramural psychiatry.

Under a grant from the Commonwealth Fund:

Dr. Grace E. McLenn of the Pilgrim State Hospital, Brentwood, N. Y., to the Cleveland Child Guidance Clinic.
Dr. John A. Rose, Ithaca, N. Y., Cornell Student Health Service, to the Philadelphia Child Guidance Clinic.
Dr. John Russell of the Osawatimie (Iam.) State Hospital to the Los Angeles Child Guidance Clinic.
Dr. Rex E. Buxton of the Iowa State Psychopathic Hospital to the Judge Baker Guidance Center.
Dr. William B. Curtis, now on the Neurological and Neuro-surgical Service at Bellevue Hospital, to the Mental Hygiene Clinic at Louisville.

Under local provision:

Dr. William L. Holt Jr. of the Worcester State Hospital to its Child Guidance Clinic.
Dr. Norman Westlund of Traverse City (Mich.) State Hospital to the Children's Center at Detroit.

Advanced Military Course at Georgetown

Georgetown University School of Medicine, Washington, D. C., has established this year an advanced course requiring three years of study for students desiring to be commissioned in the Medical Corps of the United States Army. Lt. Col. John J. McCormick, Medical Corps, M. C., U. S. Army, has been detailed to Georgetown and will be in charge of this course.

New Members of Graduate Faculty at Pennsylvania

In the Graduate School of Medicine of the University of Pennsylvania, Philadelphia, four new members are said to have joined the faculty. They are Dr. Donald Guthrie, Sayre, associate professor of surgery; Dr. Francis F. Borzell, assistant professor of radiology; Dr. Jacob H. Vastine, assistant professor of radiology; and Charles Weyl, M.S., assistant professor of radiologic physics.

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URINARY INFECTIONS IN INFANCY AND CHILDHOOD

DIAGNOSIS AND TREATMENT

HENRY F. HELMHOLZ, M.D.

ROCHESTER, MINN.

It is my purpose in this article to give in very concise form the essentials of diagnosis and treatment of urinary infections in infancy and childhood so that definite cure may be achieved in the simple forms of infection and relief obtained in the ones complicated by stasis or focal infection before irreparable injury of the kidneys occurs.

In the acute stage the urinary infections usually manifest themselves with symptoms of fever and pyuria, while in the chronic stage they may be found accidentally. Stasis in the urinary passage that is sufficient to cause marked reduction of renal function may be present for years without infection; therefore a primary infection may be associated with permanent injury of the kidney. When the patient is an infant or a child, fever that occurs without demonstrable cause is a clue to urinary infection, and examination of the urine establishes the diagnosis. The presence of pus in urine that is obtained in the usual uncontrolled way must be checked by catheterization if the patient is a girl, and if the patient is a boy a specimen of urine must be obtained after the prepuce and meatus have been cleansed. My experience has taught me that one should not start treating a patient for a urinary infection until one is certain that an infection is present in the urinary passages. If urinary infection is present it is important to know what type or types of bacteria are causing it. There are two procedures by which this information can be ascertained: (1) staining the sediment of the centrifuged urine with Gram's stain, and (2) a culture of the urine. By the former method it is possible to determine whether the infection is the result of gram-negative bacilli, cocci or a combination of the two. By means of cultures on eosin methylene blue agar one may differentiate the various gram-negative bacilli and *Streptococcus faecalis*, and by means of cultures on blood agar one may distinguish the other forms of cocci. The varied response of bacteria to different forms of treatment requires differentiation of infecting organisms.

The importance of normal renal function in the treatment of infections is best seen in the use of those methods of treatment that are dependent on a definite acidity of the urine. A defective kidney will not

secrete a urine of sufficiently low p_H or sufficiently high concentration of the drug to be bactericidal. This may apply to only a single kidney or to both kidneys. In cases in which mandelic acid therapy is used the normal kidney may excrete a urine which has a p_H of 5.0 and contains 0.7 per cent of mandelic acid, and a kidney that is badly infected may excrete a urine that has a p_H of only 6.0 and contains 0.2 per cent of mandelic acid; the former urine is strongly bactericidal but the latter is not bactericidal at all.

With the use of the ketogenic diet, mandelic acid and sulfanilamide, it has been possible to clear up urinary infections even in the presence of urinary stasis. Thus the inability to clear up urinary infection is no longer a reason for suspecting urinary stasis. It is essential, therefore, that an excretory urogram be made in all cases of urinary infection. This appears to be the only way in which it is possible to discover the presence of urinary stasis before the kidneys have been seriously injured.

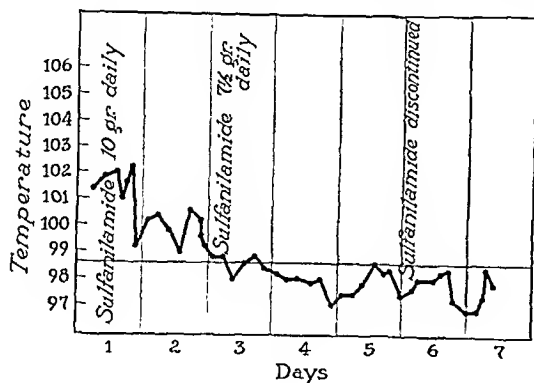
The role of focal infection is difficult to evaluate. It is certain that foci of infection in the urethra and bladder may be responsible for the recurrence of infection and that removal of such foci may effect a permanent cure. When foci of infection occur in the ureters and kidneys, they can be removed only by surgical intervention. The relationship of distant infection, for instance infection of the tonsils, to urinary infection has been claimed by many physicians but it never has been proved to my satisfaction.

If the type of infection, the renal function and the presence or absence of urinary stasis are known, the special considerations which determine the choice of urinary antiseptic are important. The ease of administration of the drug, the concentration of the drug in the urine, the p_H of the urine, the action of the drug on the various bacteria, the effect of lowered renal function and the possibility of toxic effects of the drug are the factors entering into consideration. It would seem that in a consideration of urinary antiseptics one has a wide choice, but in the last analysis two drugs stand out very prominently above the rest, namely mandelic acid and sulfanilamide.

Which of these two is the drug to use and why? Sulfanilamide has a number of very definite advantages over mandelic acid: it can be given in the acute stage of the infection, its bactericidal effect is not entirely dependent on reaction of the urine although it acts better in alkaline urine than it does in acid urine, and it is excreted in bactericidal quantities by kidneys that are so severely injured that the concentration of urea is from 75 to 100 mg. per hundred cubic centimeters of blood. The administration of sulfanilamide does not offer any special difficulties. It is taken readily by infants and older children by mouth, and when it is not

From the Section on Pediatrics, the Mayo Clinic.
Read before the Section on Pediatrics at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 15, 1938.

tolerated because of gastric irritability it can be given subcutaneously or intravenously. Its use in the acute stages of the infection, especially in infancy, is a definite advance over the previous use of only diuresis and alkalization. The chart shows a striking effect which was obtained in one case. The patient was a girl aged 8 months who had had a fever of 105 F. for a



Temperature during acute *Escherichia coli* infection in a case of pyelonephritis.

week. The kidneys were greatly enlarged; the left kidney extended to the level of the anterior superior spine of the ilium. Within forty-eight hours the temperature was normal; the kidneys decreased gradually in size and the child made an uneventful recovery.

In infections caused by *Proteus ammoniae* the urine is strongly alkaline. In the treatment of this type of

TABLE 1.—Bactericidal Effect on the *Proteus* Group of Urine Containing 51 Mg. per Hundred Cubic Centimeters of Free Sulfanilamide when Excreted

Strains of <i>Proteus Ammoniae</i>	Colonies in 0.5 Cc. of Urine	
	Before Incubation	After 24 Hours
1.....	1,820	110
2.....	1,500	0
3*.....	180	0
4.....	380	0
5.....	4,500	0
6.....	6,000	210
7.....	720	0
8.....	400	0

* *Proteus vulgaris*.

TABLE 2.—Bactericidal Action of 57 Mg. per Hundred Cubic Centimeters of Free Sulfanilamide Excreted in Urine at p_H 6.2 and 7.5

Organism	p_H 6.2 Colonies in 0.5 Cc. of Urine		p_H 7.5 Colonies in 0.5 Cc. of Urine	
	Before*	After 24 Hours*	Before*	After 24 Hours*
<i>Staphylococcus aureus</i>	770	550	230	0
<i>Escherichia coli</i>	670	3,000	680	0
<i>Aerobacter aerogenes</i>	30	4,000	Innumerable	26
<i>Proteus ammoniae</i>	700	4,000	700	0
<i>Pseudomonas</i>	2,400	7,500	3,500	1,760
<i>Streptococcus faecalis</i>	400	Innumerable

* Incubation.

infection sulfanilamide is the drug of choice because of its superior action in an alkaline urine and because of the difficulty in bringing the urine into the acid range necessary for bactericidal action with mandelic acid or methenamine. Table 1 shows the marked bactericidal effect on six strains of *Proteus ammoniae* and one strain of *Proteus vulgaris*. Table 2 shows the superior bac-

tericidal action of alkaline urine at p_H 7.5, as compared with the same urine at a p_H of 6.2, on a variety of organisms. This and numerous similar experiments seem to indicate that the urine should be rendered alkaline when sulfanilamide is administered.

A particular advantage of sulfanilamide, which deserves great emphasis, is the possible concentration that is bactericidal in the urine of patients who have injured kidneys. It has been my experience with the ketogenic diet and with methenamine and mandelic acid that an injured kidney cannot secrete a urine of low p_H , and even in those cases in which the concentration of blood urea was normal the injured kidney could not be beneficially influenced because of this difficulty. It is, therefore, striking that sulfanilamide can be excreted in the urine in sufficient concentration in cases

TABLE 3.—Use of Sulfanilamide in Sterilization of the Urine in the Presence of High Blood Urea

Case	Sex	Age, Years	Lesion	Blood Urea, Mg. per 100 Cc.	Organism	Dose of Sulfanilamide	Result
1	♀	11	Bilateral pyelo-nephritis	84-100	<i>Escherichia coli</i>	5 grains 5 times a day*	Cure
2	♀	11	Chronic pyelo-nephritis	232-300	<i>Escherichia coli</i>	5 grains 4 times a day	Failure
3	♀	10	Chronic pyelo-nephritis	68-104	<i>Escherichia coli</i>	5 grains 5 times a day*	Sterilization; relapse
4	♂	10	Bilateral pyelo-nephritis	85-100	<i>Escherichia coli</i>	5 grains 5 times a day*	Sterilization; relapse
5	♀	4	Bilateral pyelo-nephritis; cystitis	64-90	<i>Aerobacter aerogenes</i>	5 grains 3 times a day*	Sterilization; relapse

* Sodium bicarbonate given to make urine alkaline, p_H 7.0+.

† *Streptococcus faecalis*.

TABLE 4.—Absence of Effect on Five Strains of *Streptococcus faecalis* of Urine Bactericidal for *Staphylococcus* and Gram-Negative Bacilli

Strains	Colonies in 0.5 Cc. of Urine	
	Before Incubation	After 24 Hours' Incubation
1.....	1,010	Innumerable
2.....	710	Innumerable
3.....	1,080	Innumerable
4.....	160	Innumerable
5.....	270	Innumerable

in which the concentration of blood urea is well above normal. It has been possible (table 3) to sterilize the urine in four of five cases; in one of these cases the ketogenic diet and mandelic acid were employed for many weeks but the urine did not become sterile. I also wish to emphasize that the urine did not remain sterile in all these four cases. In three of the four cases the urine remained sterile for some time after administration of the drug was discontinued. This has not been possible with any other urinary antiseptic.

These very definite advantages indicate why sulfanilamide is the most useful antiseptic in the treatment of ordinary urinary infections. There is just one serious handicap to sulfanilamide as the perfect urinary antiseptic, namely its complete failure in infection caused by *Streptococcus faecalis*. For some reason *Streptococcus faecalis* is resistant to the action of the drug and will grow luxuriantly in a urine that will kill *Staphylococcus aureus*, *Escherichia coli*, *Aerobacter aerogenes*, *Proteus ammoniae*, *Pseudomonas* and other gram-negative bacilli

(table 4). Even in concentrations far above the usual bactericidal range, *Streptococcus faecalis* will grow.

Past experiences have shown that infections caused by *Escherichia coli* alone apparently cleared up under methenamine, the ketogenic diet and mandelic acid therapy, but with the disappearance of the organisms a few colonies of a streptococcus would appear on the agar plates made with 0.5 cc. of urine. In cases in which sulfanilamide was used the results have been different; in a number of instances in which *Escherichia coli* disappeared rapidly the urine was found to contain innumerable colonies of *Streptococcus faecalis*. The streptococci persisted in spite of the further use of sulfanilamide therapy but they disappeared rapidly as a result of mandelic acid therapy. Failure with sulfanilamide, as with the other urinary antiseptics, has been observed in the treatment of urinary infection associated with nephrolithiasis, postoperative wounds and indwelling catheters.

TABLE 5.—Treatment of a Boy with Bilateral Pyelctasis, Uretectasis and Cystitis Cystica

(Aerobacter Aerogenes and Escherichia Coli Infection)						
Days	Treatment	Dose		Pus, Grade	pH	Number of Bacteria in 0.5 Cc. of Urine
		Grams	Times per Day			
1	Ammonium mandelate....	1.0	4	4	...	Innumerable
4	Ammonium mandelate....	1.0	5	2	5.3	Innumerable
8	Ammonium mandelate....	1.0	5	1	...	None
11	Discontinued.....	1	...	None
12	Ammonium mandelate....	1.0	5	1	...	Innumerable
17	Ammonium mandelate....	1.0	6	1	5.2	Innumerable
19	Ammonium mandelate....	1.0	6	1	5.5	Innumerable
22	Ammonium mandelate....	1.0	6	1	5.0	Innumerable
23	Ammonium mandelate and ketogenic diet.....	1.0	6	2	...	Innumerable
26	Diet and ammonium mandelate discontinued.....
28	Ammonium mandelate....	1.0	5	3	...	Innumerable
43	Discontinued.....	3	...	Innumerable

Treatment with Sulfanilamide						
Days	Treatment	Gm.	Times per Day	Pus, Grade	pH	Number of Bacteria in 0.5 Cc. of Urine
1	Sulfanilamide.....	0.33	4	3	...	Innumerable
2	Sulfanilamide.....	0.33	4	1	...	50
5	Sulfanilamide.....	0.33	5	1	...	2
6	".....	0.33	5	1	...	0
12	".....	0.33	5	1	...	0
14	".....	0.33	5	1	...	0
16	".....	0.16	5	0	...	0
17	".....	0	...	0	...	0
19	Sulfanilamide.....	0	...	0	...	0
21	Sulfanilamide.....	0	...	0	...	0

Sulfanilamide is given in two-thirds the usual dosage for streptococcal infection; that is, 10 grains (0.65 Gm.) to 20 pounds (9 Kg.) of body weight is given daily. From four to six doses are given daily. Sodium bicarbonate is given in doses of from 30 grains (2 Gm.) to 60 grains (4 Gm.) a day. Water is usually given in the usual amounts, but the intake of fluids can be restricted if the concentration of sulfanilamide in the urine remains low. A concentration of 50 mg. of the drug in its free form in 100 cc. of urine is usually secured with this dosage. After the urine has become sterile it is essential to keep it so for a period of from four to six days and then discontinue medication. After an interval of four days, cultures are again taken to make sure that the urine has remained sterile. In a number of cases concentrations of half this amount have brought about sterilization of the urine. When the drug has been administered in this manner it has only exceptionally given rise to cyanosis and in my experience it never has caused agranulocytosis or anemia. It can be said definitely that, of the drugs at present available for the treatment of the types of urinary infection that have been mentioned, sulfanilamide is the most easily admin-

istered and the most useful drug except in cases in which the infection is with *Streptococcus faecalis*. An outline of treatment is shown in table 5.

The field of mandelic acid has been narrowed considerably by sulfanilamide, but the former drug still is very useful not only in streptococcal infections but also because of its effect on all bacteria, cocci and bacilli

TABLE 6.—The Bactericidal Effect of Mandelic Acid on *Streptococcus Faecalis* at Various Concentrations and pH

Concentration of Acid, per Cent	pH of Urine	Strains				
		1	2	3	4	5
0.25	5.0	—	+	+	+	+
0.5	5.3	S	+	+	+	+
1.0	5.5	+	+	+	+	+

—, organisms not killed; +, organisms killed; S, bacteriostasis.

TABLE 7.—Treatment of a Girl Aged 3 Years with Pyelitis of Four Weeks' Duration

Ammonium Mandelate (1.5 Gm.) Four Times a Day		
Days	pH of Urine	Escherichia Coli
1.....	...	Innumerable
2.....	5.0	0
3.....	5.2	0
5.....	...	0
6.....	Medication discontinued	0
13.....	...	0

alike; when a proper concentration of the acid in the urine and a proper pH of the urine are obtained it is a most dependable drug. As determined in vitro and therapeutically, it acts equally well in bacillary and in coccic infections. Its marked bactericidal effect on *Streptococcus faecalis* is shown in table 6. It is difficult to administer in the acute stage of urinary infections but its administration in enteric coated capsules and in suppositories makes it available in all cases in which acidification of the urine is possible. In *Proteus ammoniae* infections strongly alkaline urine and the lowered renal function render proper acidification of the urine difficult; therefore, mandelic acid is often of little use in infections of this type. In all infections in which the concentration of mandelic acid in the urine reaches from 0.5 to 1 per cent and the pH of the urine is 5.5 or less, the drug sterilizes the urine rapidly.

TABLE 8.—*Streptococcus Faecalis* Infection Cured with Mandelic Acid

Days	Treatment	Dose		Pus, Grade	Sulfanilamide, Mg. per 100 Cc. In Urine		Organisms in 0.5 Cc. of Urine
		Gm.	Times per Day		Free	Conjugated	
1	Sulfanilamide.....	0.33	6	2	Innumerable
2	Sulfanilamide.....	0.33	6	1	900
3	Sulfanilamide.....	0.33	6	1	52	31	Innumerable
5	Sulfanilamide.....	0.33	6	1	18	68	Innumerable
6	Ammonium mandelate..	1.0	4	1	Innumerable
9	Ammonium mandelate..	1.0	4	0	0
11	Medication discontinued	0	0
14	Medication discontinued	0	0
23	Medication discontinued	0	0

Mandelic acid is administered as the elixir of ammonium mandelate, as calcium mandelate by mouth, or as ammonium mandelate in suppositories. It is given in doses that will produce a concentration of from 0.5 to 1 per cent of the drug in the urine. At the clinic we administer 1 Gm. for each hundred cubic centimeters of urinary output in the twenty-four hours.

As most of the mandelate is excreted in the urine, a concentration of approximately 1 per cent will result. The p_H of the urine can be repeatedly tested by the patient with nitrazene indicator papers. A p_H of 5.5 or less is necessary for prompt action of the drug. I have repeatedly seen the urine become sterile in a period of less than twenty-four hours (table 7). It is advisable to continue the administration of the drug for five or six days after the urine has been rendered sterile, so as to kill the organisms which may be present in the various layers of the mucous membranes, and then to discontinue the medication. After an interval of four days, cultures should be taken again to make certain that the urine has remained sterile. It is well to carry out a routine such as is shown in table 8.

When the infection has been cleared up it is essential to eliminate urinary stasis if it is present. This is a matter of the utmost importance to the future health of the patient and should not be put off as it is so likely to be when the infection has been cleared up. It was possible to show with animals that so long as no stasis is present there exists an efficient barrier to the progress of an infection of the pelvis to the parenchyma of the kidney. In cases in which infection recurs periodically, it is also important to search for local foci of infection in the urethra, bladder and upper part of the urinary tract. This work should be done by a competent urologist.

SUMMARY

The diagnosis of urinary infection must include the type of infection, the state of urinary drainage and renal function, as well as the presence of foci of infection in the urinary tract. Sulfanilamide is the drug that at present meets the greatest number of conditions successfully. Mandelic acid succeeds in infections in which the necessary acidity and concentration of the drug can be obtained, including *Streptococcus faecalis* infection in which sulfanilamide fails. No patient should be dismissed as cured unless normal drainage is known to be present in the urinary passages.

ABSTRACT OF DISCUSSION

DR. WILLIAM P. HERBST, Washington, D. C.: I am interested in discussing the importance of three phases of this problem of urinary infection: first, the urgent necessity for careful study of children who have had pyelonephritis; second, general resistance in infections, and, finally, the problem of myoneural dysfunctions of the bladder. Last year at Atlantic City, Wharton, Gray and Guild presented their follow-up studies on thirty young women who had had pyelonephritis in infancy or childhood and stated that six of nine who had had only one attack and eleven of twenty-one who had had multiple attacks were the victims of definite abnormalities as sequelae. These observations demand that a study be made of every child who has only a single attack of pyelitis. Abnormalities were found in 66% per cent of the children who had a single attack. During the acute attack is no time to carry out these studies. After the acute stage is over and the little patient has regained strength, the following regimen should be instituted: 1. Careful urinalysis with stain and cultural bacteriologic study. 2. Phenolsulfonphthalein excretion test following intravenous injection. 3. Check of bladder function. 4. Intravenous urography. This is not a very disturbing examination and yet it is comprehensive enough to bring to light conditions of any importance. It not infrequently happens that patients are so interesting from a diagnostic or bacteriologic standpoint that the simple problem of building up the general resistance is lost sight of. This should not be, for, after all, whether the patient survives or not depends solely on this factor. Vitamins and hematins should be admin-

istered in generous quantities. Dr. Helmholtz has pointed out the importance of obstruction, and it happens that myoneural dysfunction of the bladder is one of the most important entities in this problem. A few simple observations which any one can make quickly can demonstrate the presence of myoneural dysfunction, which should then call for a much more detailed elaborate cystometric and neurologic investigation. First, observe how the patient voids. Any abnormality of this act is very suggestive. Second, catheterize the patient with a catheter thoroughly lubricated and also small enough to minimize the resistance factor. The status of the sphincter action can be determined by the sense of resistance that is experienced. Third, determine the presence of residual urine. Lastly, observe the force of the urine as it emerges from the catheter and see at what height above the level of the bladder the flow of urine stops. Nothing could be simpler than these few homely observations and yet such an examination is adequate to recognize the presence or absence of myoneural dysfunction, which if obstructive is important in causing and continuing urinary infections.

CHRONIC EFFECTS OF INGESTED LEAD AND ARSENIC

A REVIEW AND CORRELATION

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The purpose of this communication is to review some of the observations presented in other papers containing the experimental details in order to correlate them with one another and with observations from the literature. Our primary interests are the comparative behavior of lead and arsenic when their salts are administered at different levels to the same species or to different species, and the correlation of physiologic and pathologic observations with results from chemical analyses.

It has been evident for some time that more extensive studies of the chronic toxicity of lead and arsenic are necessary. The growing insect infestation of fruits and vegetables has necessitated the increasing use of poisonous sprays, especially lead arsenate and calcium arsenate. The use of these has led to the serious question of whether the residues remaining on these commodities constitute a health hazard.

In formulating a law enforcement policy under the Food and Drugs Act, officials of the Department of Agriculture recognize that they were without sufficient experimental evidence to permit the establishment of wholly satisfactory tolerances for lead and arsenic. The department, therefore, in January 1927 called on a committee¹ to advise it as to just what levels of lead or arsenic content in food or drink could be considered free from hazard.

In addition to recommending temporary tolerances for lead and arsenic, this committee recommended, among other things, the study of chronic intoxication by both lead and arsenic, in particular in the form in which they are used in sprays and consumed with fruits and vegetables and other food products.

Funds for such an investigation finally became available in 1935, and a division of pharmacology was

From the Division of Pharmacology, Food and Drug Administration, United States Department of Agriculture.
Read before the Section on Pharmacology and Therapeutics at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 17, 1938.

This is a brief summary of the work carried out in this division by a large group of investigators. The experimental procedures and results are reported separately in a series of publications in other journals.
1. This committee consisted of Drs. Reid Hunt, chairman, C. L. Alsberg, A. S. Loevenhart, Haven Emerson, Carl Voegtlin and F. B. Flinn. Dr. A. J. Carlson, although designated a member of the committee, could not attend.

established in the Food and Drug Administration. The first problem of research assigned to the division was a study of the chronic toxicity of lead and arsenic.

The Secretary of Agriculture also asked the National Academy of Sciences to appoint an advisory committee² on questions relating to this problem.

It was clearly recognized in the beginning that, although both forms of toxicity are caused by lead and arsenic, the question here was one of chronic and not one of acute toxicity. The real problem was to determine the minimum amounts of lead and arsenic that, when ingested periodically, would cause effects which could be attributed directly to these elements. It is clearly evident that the tolerances—that is, the amounts which may be permitted—should be below this level.

An extensive survey of the literature did not reveal the answer, although extremely valuable suggestions and helpful information were obtained. There are forty citations in the literature in which scientists have expressed themselves on the minimum amount of lead which, when ingested daily, would be dangerous.³ Of these, eleven considered that 0.005 grain (0.325 mg.) of lead a day is dangerous, twenty-one considered 0.01 grain (0.65 mg.) dangerous, thirty-two considered 0.015 grain (0.975 mg.) dangerous, and thirty-six considered 0.02 grain (1.3 mg.) dangerous. The average American food consumption is 3 pounds (1,360 Gm.) a day. If only one third of this quantity contained the amount of lead at present permitted, it would contain, in the opinion of thirty-six of these forty authors, dangerous amounts of lead. Since the methods formerly were inadequate for quantitative determination of lead, one must consider the values mentioned by these authors in the light of present day methods and remember that there was a small amount of lead present which they did not recognize. In other words, these were the determinable values by their methods and were amounts over and above the undetermined lead. The medical and scientific literature since 1616 contains more than 10,000 references to lead and a similar number to arsenic, most of which are discussions, reports of cases and studies of acute toxicity. In no instance has it been definitely established in a single species of animal just how little arsenic or lead will cause chronic toxicity when ingested over long periods.

It will suffice at this time to cite only a few of the more important individual contributions, summaries and reviews of the literature on lead from which detailed references may be obtained. Although some experimental work was done as early as 1814, most of it has been done within the last thirty years, and excellent reviews have been published by Legge and Goadby⁴ in 1912, by Oliver⁵ in 1914, by Teleky, Gerbis and Schmidt⁶ in 1919, by Blansdorf⁷ in 1922, which alone

contains about 3,000 references, and by Hamilton⁸ in 1925. The contributions of Kehoe and his co-workers⁹ have not been summarized. The book by Aub and his co-workers¹⁰ contains an excellent summary and review, as well as much original work that has had an important influence on the clinical treatment of lead poisoning. The book by Nye¹¹ on lead and its relationship to chronic nephritis is already recognized as a classic. And, finally, there is the remarkably thorough and complete review written by Flury.¹² An excellent review of the literature on arsenic from 1846 to 1919 was published in the form of a book which consists of nineteen separate reports and contains also 106 pages of results obtained by the Swedish commission on the chronic toxicity of arsenic.¹³ More recent reviews were published by Heffter and Keeser.¹⁴

Our problem was to determine the toxicity of lead and arsenic when used as sprays and as spray residue. Since it was essential to know the effect of lead and arsenic separately as well as in combination, we selected as salts for initial investigation lead arsenate, calcium arsenate, lead acetate and arsenic trioxide. The experimental procedures and details are published elsewhere.

PROCEDURE AND TECHNIC

Numerous preliminary and exploratory experiments extending over a period of almost one year, not reported in this investigation but in some instances indicated, have shown that special attention must be given to methods that are sensitive for very small amounts of lead and arsenic, constituents of the diet, housing equipment and manner of feeding. We have found it impossible to select an adequate diet entirely free of lead and arsenic.

The dithizone method was extensively studied and made applicable to the determination of very small amounts of lead in biologic materials.¹⁵

A simple research method was developed for the determination of arsenic and applied to numerous types of food and biologic tissues.¹⁶

A method for the determination of the enzyme arginase was made applicable to the determination of the effects of toxic substances in general on protein metabolism.¹⁷

The use of a method for counting the nucleated cells of bone marrow was developed and extended.¹⁸

There was confirmation of the value of and extension of the use of the hydrogen sulfide technique for localization of lead, in the bones especially, as well as in

2. This committee consisted of Drs. A. J. Carlson, chairman, Torald Sollmann, Ludwig Hektoen, H. C. Sherman and Cecil K. Drinker. The committee held its first meeting in Washington, D. C., Dec. 30 and 31, 1936, and from that time on gave its services freely and ungrudgingly. Members of the committee were also available for individual consultation. Their advice and help in connection with this investigation and other problems involving the work of the division are sincerely appreciated by members of the division and by the Food and Drug Administration.

3. In this statement it is understood that the authors considering 0.005 grain of lead a day dangerous would also consider 0.01 grain dangerous and likewise 0.015 grain dangerous would also consider 0.02 grain dangerous. Each succeeding number includes the immediate

4. Legge, T. M., and Goadby, K. W.: *Lead Poisoning and Lead Absorption*, London and New York, Edward Arnold, 1912.

5. Oliver, T.: *Lead Poisoning*, London, H. K. Lewis, 1914.

6. Teleky, L.; Gerbis, H., and Schmidt, P.: *Die Frühdiagnose der Bleivergiftung*, Berlin, Julius Springer, 1919.

7. Blansdorf, E.: *Bleiliteratur* Schriften aus dem Gesamtgebiet der Gewerbelygiene, New Series No. 7, part 2, Berlin, Julius Springer, 1922.

8. Hamilton, Alice: *Industrial Poisons in the United States*, New York, Macmillan Company, 1929.

9. Kehoe, R. A., and others: Several articles published in *THE JOURNAL* and the *Journal of Industrial Hygiene and Toxicology* since 1925.

10. Aub, J. C.; Fairhall, L. T.; Minot, Anne S., and Reznikoff, Paul: *Lead Poisoning*, Medicine Monographs, Baltimore, Williams & Wilkins Company, 1926, vol. 7.

11. Nye, L. J. J.: *Chronic Nephritis and Lead Poisoning*, Sydney, Australia, Angus and Robertson, 1933.

12. Flury, Ferdinand: *Lead*, in Heffter, Arthur, and Heubner, Wolfgang: *Handbuch der experimentellen Pharmakologie*, Berlin, Julius Springer 3: 1575-1889 (pt. 3) 1934.

13. Arsenikkommissionen Betäkande, Uppstäcka, Förbyggga och Motverka Faran äve Kronisk Arsenikförgiftning, Lund, 1919.

14. Heffter, Arthur, and Keeser, E.: *Arsen und seine Verbindungen*, *Handbuch der experimentellen Pharmakologie* 3: 463-532 (pt. 1) 1927. Keeser, E.: *Arsen und seine Verbindungen* *Handbuch der experimentellen Pharmakologie* 3: 162-197 (suppl.) 1937.

15. Laug, E. P.: The Application of the Dithizone Method to the Determination of Lead in Biological Materials, *J. A. O. A. C.* 21: 481-487 (Aug.) 1938.

16. Morris, H. J., and Calvery, H. O.: Quantitative Determination of Arsenic in Small Amounts in Biological Materials, *Indust. & Engin. Chem.* 9: 447 (Sept.) 1937.

17. Lightbody, H. D.: Variations Associated with Age in the Concentration of Arginase in the Livers of White Rats, *J. Biol. Chem.* 124: 169-178 (June) 1938.

18. Farrar, G. E., Jr.: The Concentration of Nucleated Cells in the Bone Marrow of the Albino Rat, *Am. J. Physiol.* 117: 4 (Dec.) 1936.

other organs and tissues.¹⁹ By this technic it can be determined whether the lead is in the nucleus of the cell or in the protoplasm surrounding the nucleus.

Glass cages, a description of which has been published,²⁰ were found essential for some of the phases of this investigation.

Two facts must be clearly pointed out regarding the results of these investigations: First, it must be emphasized that in all the experiments on rats, with the exception of one group, a painstaking effort was made to furnish the animals with a diet adequate in all respects, especially with regard to calcium and phosphorus. The second point which must be emphasized is that the diets fed our experimental animals were all dry diets and, especially in three of our diets, the caloric content was extremely high per gram of dry weight. This is very significant for interpretation in terms of the average human dietary, which is high in moisture. As a result of this consideration, one must keep clearly in mind that the number of grams of diet ingested by our experimental animals was relatively much less than would have been ingested had the diet had a water content comparable to that of fresh fruits and vegetables. As a result, the amounts of lead and arsenic ingested are probably from one half to one fifth as much (the lead and arsenic were expressed as milligrams per kilogram of whole diet) as would have been ingested had the animals been subsisting on diets with a water content comparable to the human dietary.

DISTRIBUTION AND STORAGE

Lead.—The amount of lead stored is directly dependent on the level of intake. This was true for the range of levels studied (from 0.61 to 2,640 mg. per kilogram of diet) even at the lowest levels. For example, one group of control rats on a diet containing 0.61 mg. of lead per kilogram contained an average of 0.88 mg. of lead per kilogram of dry weight, while another group receiving a diet containing 0.73 mg. of lead per kilogram stored an average of 1.23 mg. per kilogram of dry weight. Likewise two groups of rats fed diets containing 3.53 mg. and 2,640 mg. of lead per kilogram stored respectively 1.45 and 291 mg. per kilogram of body weight.²¹ Similar comparisons can be made on dogs only for individual animals. Dog 4, which was fed for 229 days the control diet containing 2 mg. of lead per kilogram, stored in the femur 77 mg. and in the kidney 7.5 mg. per kilogram of dry weight. Comparable figures for two litter mates of this dog (dogs 6 and 7) fed for 140 and 167 days a diet containing 14.8 mg. of lead per kilogram were, respectively, 469 and 506 for the femurs and 32.7 and 31.4 for the kidneys.²²

Our investigations have shown conclusively that lead when ingested with the diet is absorbed and stored both in the skeleton and in the soft tissues, even at the lowest levels used by us in both dogs and rats. The evidence indicates that the accumulation was continuous throughout the duration of our experiments (356 days). For example, two dogs fed for 230 days on a diet containing 2 mg. of lead per kilogram stored in the

femurs 68 and 77 mg. of lead per kilogram of dry weight respectively, whereas three dogs on the same diet for 350 days stored 125, 99, and 127 mg. respectively.²² This is in agreement with the observations of Tompsett,²³ who has studied the distribution of lead in human bones. These accumulations of lead in the tissues, as demonstrated by more sensitive methods, might possibly be the cause of chronic poisoning, as well as a cumulative injury produced by small amounts of circulating lead, as postulated by Straub²⁴ and by Erlennmeyer.²⁵

The storage of lead in the bones of young animals is much more rapid than in more mature animals. This was demonstrated very strikingly by the analyses of the femurs of a group of dogs all on the same level of lead intake (64 mg. per kilogram of diet) but placed on this diet at different ages. The average value for six young animals (from 51 to 84 days of age when placed on the diet) was 1,265 mg. per kilogram of dry weight; for two dogs about half grown (208 and 226 days of age when placed on the diet) the values were 667 and 415; for mature dogs the values were 194 and 244.²² These differences were further emphasized by the fact that the younger dogs were on the experimental diet just half as long as were the mature dogs.

The type of diet also influences the amount of lead stored. This was clearly demonstrated in two dogs of the same litter on diets identical except for calcium content and containing 64 mg. of lead as lead arsenate per kilogram. The dog receiving 0.13 per cent calcium stored twice as much lead as the one receiving 0.28 per cent calcium. Rats placed on diets (with added lead arsenate) similar, except for calcium content,²⁶ showed that the animals receiving the diet low in calcium (0.13 per cent) stored in the femurs over six times as much lead as the ones on the diet high in calcium (0.53 per cent), both diets containing approximately 2 mg. of lead per kilogram. Another series of rats receiving the same respective low and high calcium diets but with 64 mg. of lead per kilogram showed that the animals fed the low calcium diet stored about five times as much lead as the others. Approximately the same ratio (about six times) held when the diet contained 512 mg. of lead per kilogram. The storage of arsenic was just the reverse of the lead but the ratios were not quite so large. Litter mate rats definitely known to be rachitic were placed at 41 days of age in pairs on the same rachitogenic diet containing three different levels of lead, namely 512, 128 and 12.8 mg. per kilogram, and were maintained on this diet for fifty days. The diet of one member of each pair was supplemented with halibut liver oil containing viosterol. The member of each pair receiving the supplement and 512, 128 or 12.8 mg. of lead per kilogram of diet stored in the femur in micrograms per gram dry weight respectively approximately 9 (1,427 and 164), 2.5 (430 and 171) and 1.6 (53 and 34) times its pair mate.²⁷ There was no significant difference in the amount of lead stored when the diet contained either lead arsenate or lead acetate.

19. Sieber, Erhard: *Histochemischer Bleinachweis in Knochen*, Arch. f. exper. path. u. Pharmacol. 181: 273-280 (March) 1936.

20. Laug, E. P., and Calvery, H. O.: *An Improved Glass Metabolism Cage for Small Animals*, J. Lab. & Clin. Med. 22: 521-522 (Feb.) 1937.

21. Laug, E. P., and Morris, H. P.: *The Effect of Lead on Rats Fed Diets Containing Lead Arsenate and Lead Acetate*, J. Pharmacol. & Exper. Therap., to be published.

22. Calvery, H. O.; Laug, E. P., and Morris, H. J.: *The Chronic Effects on Dogs of Feeding Diets Containing Lead Acetate, Lead Arsenate and Arsenic Trioxide in Varying Concentrations*, J. Pharmacol. & Exper. Therap., to be published.

23. Tompsett, S. L.: *The Distribution of Lead in Human Bones*, Biochem. J. 30: 345-346 (April) 1936.

24. Straub, H.: *Azidose des Blutes bei Urämie*, München. med. Wchnschr. 61: 5-6 (Jan.) 1914.

25. Erlennmeyer, Emil: *Der Mechanismus der chronischen Bleivergiftung nach experimentellen Studien*, Ztschr. f. exper. Path. u. Therap. 14: 310-334, 1913.

26. Grant, R. L.; Calvery, H. O.; Laug, E. P., and Morris, H. J.: *The Influence of Calcium and Phosphorus on the Storage and Toxicity of Lead and Arsenic*, J. Pharmacol. & Exper. Therap., to be published.

27. The rachitic rats were furnished us by Dr. Rebecca Hubbell of the Connecticut Agricultural Experimental Station, New Haven. The other data are unpublished results from this laboratory.

There is storage of lead in all tissues of both species, and in some tissues the amount is enormous, especially at relatively high levels of intake. The amount stored does, however, vary, as already mentioned, with the calcium content of the diet.

Arsenic.—There is storage of arsenic even at the lowest level of arsenic concentration in the diet (0.07 mg. of arsenic per kilogram of diet), and a much greater storage following ingestion of diets with a higher arsenic content (215 mg. of arsenic per kilogram of diet). There was a difference in the amount of arsenic stored when different salts were fed at the same level, much more being stored when calcium arsenate was fed than when arsenic trioxide was the source of arsenic.²⁸ There was likewise a marked species difference, the dog storing much less than the rat, even when on the same levels of intake for longer periods of time.²² There is a definite indication from these experiments that arsenic is not stored in anything like the amounts in which lead is stored.

The maternal transfer of both arsenic and lead as reported by other investigators¹² has been confirmed by chemical analyses of a large number of rats at birth, and of dogs. Chemical analysis has also demonstrated a higher content of lead in the milk of a dog receiving added lead in the diet than in that of a dog on a diet containing no added lead.²² The lead content of rats at birth was the same per gram of dry weight as at 15 days of age (at this age they had not partaken of food other than the mother's milk), although their increase of weight was more than 500 per cent. This was not true for the arsenic content, which was from five to ten times greater per gram of dry weight at birth than at 15 days of age.²⁹

Although in this series of investigations we have studied only the retention of lead and arsenic in two species of animals, quite extensive studies have been reported in the literature of storage in other species and in human beings. The distribution and storage of lead is fully considered by Aub and his co-workers,¹⁰ Flury,¹² Legge and Goadby,⁴ Nye,¹¹ Behrens and Baumann,³⁰ Tompsett²³ and Kehoe and his associates.⁹ The last named authors have made a very significant study on man.³¹ On two different occasions they studied the lead balance of an individual before lead was fed. One mg. of lead was given daily during a period of ten days, and the urine and feces were analyzed for the following sixteen days. The total lead ingested, including that in the food, was 14.2 mg. The lead retained was 4.52 mg., or 31.9 per cent of that ingested. In the second experiment, 5 mg. of lead was ingested daily for six days, a total of 30 mg. of added lead plus 2.3 mg. in the diet. The feces and urine were analyzed for thirty days before and for sixty-four days following the ingestion. The amount of lead retained was 7.62 mg., indicating quite clearly that the tissues held tenaciously to a considerable portion of the lead presented to them. This is extremely important, in view of the fact that

Aub and his co-workers¹⁰ and others³² have shown that immobile stores of lead may be rendered mobile by alterations of the diet and by this means acute attacks of lead intoxication may be caused.

The paper of Dr. Kehoe and his co-workers,³³ which indicates that an equilibrium is established under certain conditions when the lead intake of individuals is controlled, is an excellent type of experiment. In this type of experiment, like that in which one is accurately controlling the fluid intake of individuals when one is determining water balance, it is required that extreme care be taken to measure all intake and all output. This is especially true when one is considering small differences between intake and output. The storage of lead on very low intake would be expected to be very small and, as a result, extreme care should be taken to know every source of possible intake and the amounts. In the experiment of Kehoe and his co-workers, the lead intake in the water was not mentioned, although it may have been considered with the food, and likewise the individuals were not housed during the experiment in such a way that the lead content of the inhaled air could be taken into consideration. cursorily these sources of lead might seem of little significance, but when one is discussing equilibrium one must inevitably consider all factors. Numerous analyses of city water have shown that lead is always present. What we have analyzed averages 3 micrograms per liter, and lead from this source alone would lead to an intake of from 6 to 12 micrograms a day or probably more. Because of the lead content of the dust of the air even in air conditioned rooms, we were unable to do accurate lead balance experiments on animals when the lead intake in the food was from 0.61 to 3.53 parts per million.²¹ In this connection the increasing storage of lead with age in the femur of human beings as shown by the investigations of Tompsett²³ are of particular significance, as are also the results of our investigation on animals.

PHYSIOLOGY

Growth.—The effect on growth was studied only in the rats. There was no significant effect caused, we feel, by the levels of arsenic fed. In the case of lead (with adequate calcium in the diet) there was an effect on growth of the males attributable to added lead at each level. This was true at only one level for the females, in which case they were the offspring of a parent generation which had been fed a diet with the same added level of lead. With no great effects at the very high level of 2,640 mg. per kilogram of diet, it is surprising that the results are statistically very significant in the case of males fed diets containing 3.53 mg. of lead per kilogram. As would be expected, the relative amount of lead absorbed and stored by animals on the two diets was much higher for those on the 3.53 mg. level. This is in agreement with the observations of Sollmann,³⁴ who reported that very low levels showed, under the conditions of his experiment, greater effect on growth than somewhat higher levels. We have no explanation to offer as to why this should be the case in our series of investigations other than the fact that the lead, which was added at the lowest level,

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31. Kehoe, R. A.; Thamann, Frederick, and Cholak, Jacob: On the Normal Absorption and Excretion of Lead: II. Lead Absorption and Lead Excretion in Modern American Life. *J. Indust. Hyg. & Toxicol.* 15: 273-288 (Sept.) 1933.

32. Gray, Irving: Recent Progress in the Treatment of Plumbism. *J. A. M. A.* 104: 200-205 (Jan. 19) 1935.

33. Kehoe, R. A.; Thamann, Frederick, and Cholak, Jacob: Normal Absorption and Excretion of Lead: *J. A. M. A.* 104: 90-92 (Jan. 12) 1935.

34. Sollmann, Torald: Studies of Chronic Intoxications on Albino Rats: VI. Lead Carbonate. *J. Pharmacol. & Exper. Therap.* 10: 375-384 (June) 1922.

was in the form of lead arsenate, while at all other levels the added lead was in the form of lead acetate. However, our results²⁹ show that calcium arsenate and arsenic trioxide did not have this effect, while it was shown that lead acetate and lead arsenate were equally toxic to dogs at the levels fed.²²

Food Intake.—The effect on food intake of added lead and arsenic to diets fed young rats is comparable to that found for growth. There was, in many of the experiments, a restricted food intake caused by the added lead in the diet, especially at the higher levels. This was also true for the diets containing arsenic and was especially marked at high levels. We have not enough data to determine definitely whether there was a different food intake when lead acetate was compared to lead arsenate, except at very high levels. Under those circumstances there is much greater restriction and a much greater effect when lead arsenate is present than when lead acetate is present. The effect on food intake of dogs was shown only in the case of lead. The levels of arsenic fed produced no effects. Anorexia, however, was one of the early symptoms of the effects of lead on the animal.

Reproduction.—Rats: Reproduction was studied most extensively in rats.²⁹ This was followed through four litters of the first generation and one litter of the second generation. The studies were made on equal numbers of paired litter mate experimental and control animals, and observations were made on the number of litters born, the average number of young in each litter, the survival and weight gains and the weight gains and food consumption of the dams. There was no significant difference noted in the fertility and fecundity between the experimental and the control rats. Nor was there any significant effect noted on the ability of the dams to rear their young or in the mortality up to the time of weaning at 21 days of age. The dams consumed essentially the same amount of food during the lactation period in all the groups, and their weights remained practically constant during the lactation period.

Dogs.—The effect on reproduction in dogs was noted only in two instances.²² In the first instance, a mature female which had previously given birth to a litter of six pups was again bred after she had been on a diet containing added lead acetate for only one week. Even though the mother, near the end of the gestation period, showed mild symptoms of lead poisoning, six apparently normal pups were born. In the second instance a young female was bred which had, as a pup, shown severe signs of lead poisoning in the form of paralysis. She had been removed from the lead diet for an interim period of 212 days and was then returned to the lead-containing diet for approximately eighty-five days before being bred. At the end of the gestation period, when she failed to give birth to pups, she was killed, and on examination of the uterus definite evidence was found of resorbed fetuses. Although this is a single instance, it is in accord with the generally accepted view that in human beings lead shows its influence in pregnancy in a similar manner or by abortion.

ENZYMOLOGY

In conjunction with the other studies made in this investigation, the effect of lead and arsenic on an enzyme system was included. This system was the arginase system of the rat's liver.¹⁷ It was selected

because of the generally accepted view that it is directly involved in intermediary protein metabolism, specifically in the formation of the end product, urea. By this means it was felt that if there was an effect on protein metabolism caused by the ingestion of lead and arsenic it could be indirectly measured by study of the concentrations of this enzyme, since the liver arginase concentrations following daily intraperitoneal injections of lead or arsenic were less than those of controls. Animals that had had their general metabolism interfered with by fasting showed a lower rate of protein catabolism, as measured by arginase concentration, when given lead or arsenic. Animals that had been given small quantities of lead with their food over long periods of time also showed a lower rate of protein catabolism after fasting. This was not true of animals fed foods containing arsenic. The concentrations of the enzyme in the livers of sucklings whose mothers were fed foods containing lead and arsenic were found to be significantly lower than those of controls whose mothers were fed similar foods containing no lead or arsenic.

TOXICOLOGY

Lead.—The toxicology of lead has been extensively discussed by Aub and his co-workers,¹⁰ by Flury,¹² by Nye¹¹ and by Legge and Goadby,⁴ as well as by other investigators.³⁵ In our investigations, signs of lead intoxication were exhibited in both species of experimental animals but were most marked in the dogs. These animals exhibited many of the usual symptoms recognized in cases of human lead poisoning. Quite often they were restive or moody, showed loss of appetite, irritability, tremors and twitchings, paralysis from the mild to the severe forms and encephalopathy with severe convulsions. In some cases there was hematuria, and the blood changes noted were the increase of reticulocytes, stippled cells and anemia. These responses were noted both with lead acetate and with lead arsenate and at the lowest level of added lead, namely 12.8 mg. (total 14.8 mg.) per kilogram of diet, or only five times the present tolerance specified by the government, in which case the animals received only 0.33 mg. of lead per kilogram of body weight daily. As evidence of lead intoxication in the rats, very few of the usual symptoms were observed, among which were anemia, stippled cells and restricted food intake. As already mentioned, a survey of the literature revealed that thirty-six of forty investigators considered 1.3 mg. of lead per day to be dangerous for human consumption. In this connection, Sollmann³⁴ has made the following statement:

These data show that daily doses of 0.01 to 0.03 mg. per kilogram are said to produce poisoning in man, but with doubtful data. Absorption of 0.1 mg. per kilogram per day from hypodermic injections does not poison cats, even in twenty-four weeks (Erlenmeyer).

Daily absorption of 0.2 to 0.3 mg. per kilogram appears to be the usual dosage in human lead epidemics from leaden water-pipes, where the dosage can be rather definitely calculated from the lead content of the water (12 to 20 mg. of lead per liter; Brouardel).

Daily absorption of 1 to 1.5 mg. per kilogram (from hypodermic deposits of lead carbonate, Erlenmeyer and Straub) is the smallest dosage that has been shown to produce definite symptoms in animals. The symptoms occur after a latent period of about five weeks but rapidly become severe and terminate with death; i. e., they are much more severe than the symptoms of most clinical cases.

35. Hanzlik, P. J.: Health Hazards of Chemo-Enemies in Contaminated Foods, *Scient. Monthly* 44: 435-439 (May) 1937.

Daily dosage of 12 to 30 mg. per kilogram is the smallest that has been reported as producing definite symptoms in animals, by oral administration.

In our investigations on dogs in no instance did dogs receive more than 2.56 mg. of lead per kilogram of body weight daily (and this in only one instance), following which the animal succumbed on the fifteenth day of the experiment. In view of our results, it seems that the relative toxic dose for dogs of ingested lead is approximately the same as that which had been reported for human beings who have ingested lead in their drinking water. The difference observed between the relative effects of lead on rats and dogs undoubtedly is for the great part due to the fact that the rats were on what was considered an adequate diet in all respects for growth and reproduction, whereas the dogs were on a diet considered adequate except for calcium, which was purposely made relatively low for comparison of the effects resulting when a diet was used comparable in calcium content to that of a relatively large percentage of the average human dietary. The observations of Aub and his co-workers on clinical cases, as well as in animals,¹⁰ and our own preliminary observations had shown that there was a close relationship of the toxicology of lead to calcium metabolism. This was confirmed in experiments on both dogs and rats. From our results there is a definite indication that high levels of calcium in the diet exert some prophylactic effect with regard to lead intoxication, but it should be strongly emphasized that the hazard should be kept at a minimum and no attempt made to offset it by means of a possible prophylactic.

In many toxicologic investigations the deleterious effects of a substance are measured by its effect on growth and intake of food. Throughout this series of investigations we have been strongly impressed with the inadequacy of these criteria as measures of intoxication, since in many instances recognizable and even severe effects on the animal have been produced without noticeable alteration of these two factors. This is most marked by microscopic observation of kidneys of both rats and dogs receiving ingested lead, as well as by determination of the marked differences in weights of different organs in these animals and by chemical examination, especially of kidneys and bones. In confirmation of the attempt by Nye¹¹ to correlate nephritis with exposure to lead of a large proportion of the population of Australia, we have found that the organ most seriously affected by the ingestion of lead is the kidney. It should be emphasized that accurate chemical analysis of organs, tissues and body fluids is the best and probably the only adequate method at the present time of detection of exposure to lead. The development of adequate methods for determination of very small amounts of lead is probably the greatest advance that has been made in recent years for the diagnosis of lead poisoning.

Arsenic.—The toxicology of arsenic for both animals and human beings, and particularly the latter, is extensively discussed in practically all textbooks of pharmacology and toxicology, as well as in numerous summaries and reviews. Our investigations on arsenic have not been extensive enough to draw many definite conclusions. We have found, however, that the toxicity of arsenates, as measured by the ingestion of calcium arsenate, is greater than that of arsenites as measured by the ingestion of arsenic trioxide when consumed under the same experimental conditions and at the same level.

PATHOLOGY

The pathologic observations on dogs and rats, so far as they have been made, are similar in many respects to those reported by other investigators as a result of the administration of these two metals both in human beings and in laboratory experimental animals. The gross pathologic changes following administration of lead included anemia, stippling of red cells, hyperplasia of the bone marrow, thickening of the bones and increased hardness and brittleness, hyperemia and edema of the brain, hypertrophy of the kidneys, due both to edema and to actual hypertrophy of the tissues as demonstrated by increased dry weight. These were associated with peripheral paralysis, severe encephalopathy, convulsions and ophthalmoplegia.³⁶ By special methods of treatment the deposits of lead were converted to lead sulfide, and enormous quantities were demonstrated in the bones and cartilages, and large deposits were also seen in the kidneys. These observations have been confirmed by chemical analysis. The kidneys of the rats showed marked irregularity of the tubular epithelium with hypertrophy of the nuclei of many of the tubular epithelial cells. Many of these cells contained eosinophilic inclusion bodies similar to those described by Blackman³⁷ in the kidneys of human subjects with lead poisoning. Special treatment of the kidneys with hydrogen sulfide revealed particles of lead sulfide in the nuclei which were similar in size and position to the eosinophilic inclusion bodies previously mentioned.

It is believed that these two types of inclusion bodies may have the same origin. Similar observations were made on the dogs, except with regard to the tubular changes. Marked tubular degeneration was found in the kidneys of all the dogs examined. The type of degeneration was different, however, from that seen in the rats. The tubular epithelial cells were irregular in size, and many contained hypertrophied nuclei. Many injured epithelial cells had sloughed into the lumen. The tubular changes noted in dogs differed from those noted in the rats and observed by Blackman in the kidneys of children who had died of lead poisoning in that no eosinophilic inclusion bodies were noted. On the other hand, the damaged nuclei were broken into many fragments which were scattered throughout the cell. Many of the tubular epithelial cells were damaged in this way, and the changes were the same in material fixed with solution of formaldehyde and with Zenker fluid. The few pathologic observations made on rats receiving arsenic revealed more or less generalized capillary dilatation in the viscera and parenchymatous degeneration of the liver. The bone marrow was slightly hyperplastic. The pathologic effects noted in the animals fed calcium arsenate were similar to those receiving arsenic trioxide, except that they were more marked and included an extensive edema. This is contrary to the usual conception that arsenic in the trivalent form is more toxic than in the pentavalent form.

CONCLUSIONS

One of the most extensive studies made was the determination of storage and distribution of lead and arsenic in the organs and tissues of the animals when

36. Aub, Fairhall, Minot and Reznikoff.³⁹ *J. Surg.*

37. Blackman, S. S.: Intracellular Inclusion Bodies in the Kidney and Liver Caused by Lead Poisoning. *Bull. Johns Hopkins Hosp.* 58: 384-403 (June) 1936; Lesions of Lead and Encephalitis in Children. *ibid.* 61: 1-61 (July) 1937.

fed basic diets of known composition and the same diets to which known amounts of these elements were added. The concentrations of these in the diets ranged from a fraction of a milligram to several hundred milligrams per kilogram. There was definite storage of lead in all organs and tissues examined at all levels fed. The storage of arsenic was also shown, even at the lowest levels fed.

It was established that there are species differences in susceptibility to the toxicity of these deleterious substances.

One of the original plans of this investigation was to vary the concentration of certain essential constituents of the diet in order to determine whether such variation had an influence on the toxicity of these elements. This was considered essential because of the inconsistency of the human dietary. During the course of the study it was strikingly and conclusively demonstrated that variation of the calcium content from a low level approximating that of a large percentage of the human dietary to a higher level markedly influences the storage and toxicity of lead, and it was also demonstrated that a variation in the calcium to phosphorus ratio influenced the storage of arsenic.

At the levels fed in this investigation, calcium arsenate was more toxic and caused greater storage than did arsenic trioxide at the same level.

There was no difference observed in the toxicities of lead acetate and lead arsenate when fed at the same relatively low levels, but at high levels the lead arsenate was the more toxic.

Even at the lowest level of added lead (2.566 parts per million, total 3.53 parts per million), there was a significant effect on the growth rate of male rats and on both males and females at higher levels. In some cases there was also an influence on the intake of food.

No significant differences were noted between the control and the experimental rats in either the P_1 or the F_1 generations on the fertility and fecundity.

Our studies decisively proved, by chemical analysis of large numbers of newborn animals, that both lead and arsenic are transferred from the mother's tissues to the fetus and also that lead is transferred in the milk. Even at the lowest levels of the intake of lead (0.61 part per million) the average concentration of lead of a large number of newborn animals was the same as that of the mother's diet.

The pharmacologic and toxicologic effects of both lead and arsenic have been further demonstrated by pathologic changes, which have not only confirmed the chemical changes but been essential in the establishment of injuries when consumption of food, rate of growth and reproduction have failed to demonstrate them. The fact that criteria other than pathologic, although often the only ones used, may fail to disclose actual injury is sufficient evidence that histologic examinations must be relied on in all toxicologic studies.

In all the animals fed diets containing added lead there was a striking effect on the size of the kidney. This was most marked in those animals on the diets having the lower calcium content. In the case of dogs, the average wet weight of the experimental organs was 140 per cent and the dry weight 97 per cent greater than the weight of those of the controls. The kidney is one of the first organs, if not the first, to show signs of injury as a result of lead in the diet.

ABSTRACT OF DISCUSSION

DR. FLOYD DEEDS, San Francisco: The investigations reported by Dr. Calvery supply definite and objective experimental evidence which is confirmatory of the clinical results already known. This evidence is important and timely in view of the adverse statements made in certain nonmedical publications regarding the injustice done to farmers by the imposition of spray residue tolerance limits. Dr. Calvery has shown that storage of lead occurs in both dogs and cats even at the lowest levels of intake used. It is safe to predict that storage would have taken place with even lower levels, but longer exposure would have been required. Storage of lead is important because under altered physiologic conditions stored lead may be released, with a consequent streaming of lead through the tissues and resulting production or exacerbation of symptoms. This leads me to emphasize the importance of streaming of lead through the tissues. Aside from specific local effects in the storage depots, stored lead may be relatively harmless; it is removed from the body, in a sense. Not so the streaming lead. Chronic toxicity is associated with cumulative injury to vital tissues by chronic exposure to a stream of lead. Cumulative poisoning is frequently regarded as synonymous with storage. It is only natural that interested groups, such as producers of insecticides and farmers, should minimize and even deny the importance of, or occurrence of, lead and arsenic poisoning. It requires much more medical knowledge to appreciate the possibilities and potentialities of chronic poisoning than to appreciate acute poisoning, which is often more easily correlated with the causative factor. One may, however, be hopeful that even these groups will become cognizant of the dangers and more cooperative when the economic aspects of the problem become acute. In the state of Washington the accumulation of the spray materials of twenty years or more is making the land toxic to many kinds of plant life. The situation is sufficiently acute to cause the state college of Washington to seek an antidote for soil poisoning. Details on this subject were published in the *Washington Farmer* for April 14, 1938. The solution of the problem is not the setting of tolerance limits and the development of antidotes for soil poisoning. These are but temporary expedients to be used while new insecticides are developed, preferably organic compounds which will be nontoxic in themselves or will volatilize or decompose under weathering conditions.

DR. ERWIN E. NELSON, New Orleans: The background for the work of Dr. Calvery and his associates should be of interest in connection with the actual presentation of the experimental results. The problem was not to demonstrate the toxicity of lead or arsenic, which is generally recognized, but to demonstrate just how much lead or arsenic must be ingested to be poisonous. Under the present federal Food and Drug Act the secretary of agriculture is authorized to issue so-called tolerances for substances such as lead and arsenic. These tolerances are advisory figures for industry as to the level below which action will not be taken against foods and drugs passing in interstate commerce. The tolerances set for lead and arsenic, set after consultation with a committee of prominent scientists, have been much criticized, on the one hand, by certain persons concerned with the public health as being too liberal and, on the other hand, by producers of certain foods, particularly fruits, as being too severe. The problem set Dr. Calvery was to extend present knowledge to the place where it could be said with assurance just what tolerance is proper to protect the public health. Some recently reported work, in which rats were the experimental animals, showed that this species will tolerate relatively large amounts of lead. Opponents of the present tolerance have frequently cited this work as evidence that the tolerance is too severe. However, there are wide species differences, and such information as is available indicates that the human species is more susceptible than laboratory animals. Actually not a great deal of information exists as to human toxic or fatal doses, in a quantitative sense, except in the case of diethylene glycol, for which the information on man and laboratory animals is fairly complete. While the work of Calvery and his associates was

brought to an end before it was completed by a specific prohibition in the appropriations for the Department of Agriculture, the demonstration that dogs were seriously and even fatally poisoned by the daily ingestion of an amount of lead five times as great as that permitted under the present tolerance would make one hesitate to approve a lowering of that tolerance.

DR. P. J. HANZLIK, San Francisco: Dr. Calvery has essentially confirmed the results of others with lead and arsenic compounds. Residents on the Pacific slope know that 60 or 70 per cent of the insecticides used in this country are sprayed on the valleys and mountain sides and on all kinds of food products there, and they have opportunities to observe interesting aspects of the health hazard problem. When one considers these features, together with experimental results, there is not much doubt that there are health hazards in spray residues. A rancher testified that he lost 5,000 turkeys by driving them through an orchard; another rancher drove his team of horses through an orchard, where they nibbled alfalfa, and later the horses died. A pest control operator said to me "What can I use in the place of lead arsenate? I am practically broke from spraying with airplanes and having some of the spray drift to adjoining ranches and having to pay indemnities for losses of cattle." Dr. Calvery has added new evidence. He has taken great pains in examining the blood and tissues. He makes a point of the increase in size of the kidney, which agrees with the results obtained with other heavy metals and is apparently a form of nephrosis. These effects seem to occur before other general physiologic reactions. He has made experiments with lead arsenate itself and confirmed known experimental and clinical effects of lead and arsenic, as well as opinions of qualified experts given in court concerning the health hazards of spray residues. He makes the point that lead is more important than arsenic in this connection, which is correct. His positive results dispose of the uncritical results of Tayloe and Talbert of the University of Missouri Agricultural Experiment Station, who claimed that lead arsenate fed to rats was not injurious and, in fact, seemed innocuous, if not beneficial. The fact is that the quantity, or dose, or the tissue concentration and the time element are in inverse relationship: the lower the dose, or the lower the tissue concentration, the longer it takes for the development of manifestations of chronic intoxication, and the greater the dose, or the higher the tissue concentration, the shorter the time for development of functional injuries. As far as tolerance limits are concerned, any one who knows the history of this problem knows that they are purely arbitrary. Dr. Calvery has shown that five times the tolerance limit for lead, which is a very low concentration in the diet, causes definite injurious effects, and he has reason to believe that the tolerance limit itself would produce effects if the poison was given long enough, and I agree with that.

Mauriceau's Book Used 150 Years.—Since obstetrics was the one specialty left open to medical women in the seventeenth century, it was not unnatural that Ambroise Paré should in 1573 write a book for French midwives and open his own house as a school for their education. But his book incurred the wrath of the surgeons of Paris because, being written in French, it gave promise of being popular. They immediately jumped to the obvious conclusion that, if midwives were well educated, they could and would undertake all sorts of surgical operations which hitherto men alone had performed. As a fact, since the beginning of the century men were being frequently called by midwives to help in a difficult or operative labor case. Mauriceau (1637-1709), for instance, went not only to the Hotel Dieu to assist the midwives there with their charity patients but also to the bedside of noble ladies during their confinements. His book on the diseases of pregnancy and the puerperium, published in 1668 and illustrated with fine copper plates, was used for a hundred and fifty years until corrected and superseded by Madame Boivin's book in the early nineteenth century.—Hurd-Mead, Kate Campbell: *A History of Women in Medicine*, Haddam, Conn., the Haddam Press, 1938.

NUTRITIONAL DEFICIENCY AND THE NERVOUS SYSTEM

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The phenomenal advances of recent years in the field of nutritional diseases have brought about a reorientation of thought and have made it evident that the older clinical classifications and nomenclature are sometimes misleading. For example, the term "pseudopellagra," which was based on an etiologic misconception, has been dropped by common consent, and that of "alcoholic" polyneuritis has been proved to be a misnomer.¹ Moreover, various other neuritides that were formerly attributed to some hypothetic toxin, and even certain cases of "infectious" polyneuritis, are now being attributed to deficient ingestion or utilization of the vitamin B complex.

RECENT OPINION

In a recent paper by Cobb and Coggeshall² the principal causes of polyneuritis were classified as in the accompanying table.

Generalized Polyneuritis

Virus	Bacteriotoxic	Deficiency or Metabolism
Measles	Focal infections	Pellagra
Smallpox	"Rheumatism"	Pernicious anemia
Chickenpox	Erysipelas	Sprue
Parotitis	Scarlet fever	Beriberi
Herpes	Rheumatic fever	"Alcoholic neuritis"
"Acute febrile"	Chorea	"Korsakoff's psychosis"
"Acute infective"	Septicemia	Pernicious vomiting
"Landry's"	Puerperal fever	Hunger edema
Poliomyelitis	Gonorrhea	Pregnancy
Encephalomyelitis	Meningitis	Chronic colitis
Epidemic (lethargic)	Diphtheria	Cancer with cachexia
encephalitis	Typhoid	Tuberculosis with cachexia
Erythro-edema	Paratyphoid fever	Senility with cachexia
Acute rabid myelitis	Typhus fever	Diabetes
	Influenza	Myxedema
	Pneumonia	Hematoporphyria
	Malaria	"Recurrent polyneuritis"
	Relapsing fever	"Chronic progressive polyneuritis"
	Serum sickness	
	Acute enteric fever	Chronic bacillary dysentery

This classification of Cobb and Coggeshall includes under the heading of "deficiency or metabolism" a large series of neuritides which would not have been so classified a few years ago. Therefore is it not reasonable to suppose that increasing knowledge may lead considerably further in the same direction? For example, why did not Cobb and Coggeshall include in the column of neuritides attributable to "deficiency or metabolism" cases developing in relation to malaria, the enteric fevers, typhus fever and, perhaps, still others which they classified as "bacteriotoxic?" The views recently expressed by several other authors are illuminating in this connection:

Wechsler³ said (p. 825):

Many cases of polyneuritis of obscure origin are probably neither toxic nor infectious in nature, at least not in the sense in which those two words are generally used, but more likely are deficiency syndromes. Even if, from their clinical appearances they cannot be regarded as cases of beriberi or pellagra,

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1. Minot, G. R.; Straus, M. B., and Cobb, Stanley: "Alcoholic" Polyneuritis: Dietary Deficiency as a Factor in Its Production, *New England J. Med.* 208:1244 (June 15) 1933. Straus, M. B.: The Etiology of "Alcoholic" Polyneuritis, *Am. J. M. Sc.* 180:378 (March) 1935.

2. Cobb, Stanley, and Coggeshall, H. C.: Neuritis, *J. A. M. A.* 103:1605 (Nov. 24) 1934.

3. Wechsler, I. S.: Etiology of Polyneuritis, *Arch. Neurol. & Psychiat.* 29:813 (April) 1933.

they might still be grouped with the avitaminoses. . . . In many cases of polyneuritis which have hitherto been regarded as due solely to a specific cause, such as alcohol, lead, arsenic or phosphorus, one finds an additional, possibly determining, factor in avitaminosis. This may be due to involvement of the gastrointestinal tract or the liver, of which there is not infrequently clinical evidence. Such a view may serve to explain why polyneuritis develops in only certain patients, although all are exposed to the same poison. . . . The fact that the general pathologic changes are degenerative rather than inflammatory and are similar to the degenerative changes seen in avitaminoses furnishes pathologic evidence of some value. . . . While in beriberi and pellagra the antineuritic vitamins B₁ and B₂, or G, are involved, in some obscure cases and in some others in which the avitaminosis seems to play the decisive role it may be that other or additional vitamins are concerned. . . . It is possible . . . that in every case in which there is a deficiency of antineuritic vitamins there must be an additional toxin or poison to bring about degenerative changes.

The growing tendency to group together neuritides that have been described as separate types is also illustrated in a paper by Harris.⁴ He suggested that various forms of recurrent or progressive polyneuritis, excepting Dejerine's familial type, should be regarded as variations and should be brought together under the descriptive term of "chronic progressive (endotoxic) polyneuritis."

Lewy⁵ writes as follows:

This presentation, which is based on clinical observations and neurologic and chemical examinations, started with the observation that, despite the clinical variety of peripheral nerve diseases, their histopathologic features are uniform. Primary inflammatory processes of the peripheral nerves are unknown. Therefore the term neuritis is erroneous and should be replaced by neuropathy. . . . The pathogenic mechanism of the neuropathy, therefore, seems to be as follows: First, various primary etiologic agents—infectious, toxic and metabolic—act on the liver. The liver cell becomes depleted of its glycogen and, simultaneously, of its vitamin B content. Then the stage is set for a neuropathy. Second, avitaminosis B appears as the only form of neuropathy. However, the neuropathy is not the only sign of avitaminosis B. In addition, there are (1) the so-called general symptoms, (2) physical signs and (3) evidence of systematic degeneration in the spinal cord and basal ganglia. The same phenomena have been found and discussed in connection with the following groups of diseases: (1) disturbances of metabolism, e. g. in diabetes, alcoholism, pregnancy, cachexia and hunger; (2) pernicious anemia; (3) poisoning with heavy metals, such as lead, manganese, arsenic and mercury; (4) infectious diseases, e. g. yellow fever, typhus, typhoid and paratyphoid, streptomycosis and diphtheria, and (5) some constitutional hereditary forms of neuropathy.

A number of interesting points were raised in the discussion of a subsequent paper by Lewy.⁶ Zimmerman⁷ said at that time:

Which chronic alcoholic patient will present clinical manifestations of pellagra and which the polyneuritis of beriberi cannot be predicted. Nor can one predict the type of anatomic changes in the nervous system. I have seen several such patients, each of whom had "axonal" changes in the ganglion cells like those associated with pellagra, pseudo-encephalitic lesions of Wernicke, degeneration of the posterior columns of the cord and demyelination of peripheral nerves.

The views and postulates of Cobb and Coggeshall, Wechsler, Lewy and Zimmerman as here epitomized show that vitamin deficiency should now be seriously

considered as a factor of possible importance in the mechanism of production of a great many cases of degeneration of the peripheral nerves, with or without evidence of cord lesions, which would have been attributed in former years to various other causes.

In this connection, I believe that to Cobb and Coggeshall's list of neuritides attributable to "deficiency or metabolism" might properly have been added some of the neuritides listed by them as "bacteriotoxic." I refer especially to neuritides occurring in typhus fever, malaria, relapsing fever and the enteric fevers. The well known increased need for vitamins that occurs in the presence of infections is a point in favor of this view. In a paper published ten years ago I⁸ showed a close analogy between the polyneuritis of beriberi and that occurring in alcoholism and in debilitating diseases of many kinds. It was said then that "some of the cases of polyneuritis developing with the above-mentioned conditions might, perhaps, be properly regarded as true beriberi and not merely as complications or sequelae of the other diseases."

In 1936 Vedder⁹ (p. 292) made the following significant statement:

Beriberi may be associated with other diseases, such as malaria and the various intestinal and pulmonary infections. Bronchopneumonia frequently is found at necropsy. It is an interesting speculation if the neuritis attributed to malaria, dysentery and other infections may not in many instances be caused by mild symptoms of beriberi. Certainly, neuritis complicating the various infections is seen more commonly in Oriental races than among Europeans. Many of these infections also are chronic and are treated with one-sided or liquid diets.

Substances contained in the vitamin B complex are known now to be of essential importance for the protection of the nervous system. It is generally recognized, too, that failure to assimilate and to utilize these substances may be as potent a cause of neurologic pathologic changes as is failure to ingest the vitamins in adequate quantity.

This concept permits the classification, as syndromes of deficiency of vitamin B, the neuritides occurring in connection with a great variety of morbid conditions.

PATHOLOGIC CHANGES OF THE NERVOUS SYSTEM IN DEFICIENCY DISEASES

The point should be emphasized here that lesions may be found in the nervous system showing cellular infiltration about the blood vessels or other phenomena which are commonly associated with, and attributable to, inflammation caused by infectious processes. There are also degenerative lesions traceable to arteriosclerosis. The frequent finding of arteriosclerotic changes in the brains of elderly pellagrins, however, does not invalidate the fact that degenerative changes have been frequently described as occurring in the brain in cases of pellagra in which there was no associated arteriosclerosis. I shall discuss only lesions of a degenerative or "neurotoxic" character which are not complicated by evidences of inflammation or arteriosclerosis.

Beriberi.—According to Vedder,⁹ the degenerative changes in the peripheral nerves may be slight or pronounced, but all peripheral nerves commonly show some

4. Harris, Wilfred: Chronic Progressive (Endotoxic) Polyneuritis, *Brain* 58: 368 (Sept.) 1935.

5. Lewy, F. H.: The Problem of Neuritis, *Arch. Neurol. & Psychiat.* 38: 222 (July) 1937.

6. Lewy, F. H.: Neurologic Aspects of B Avitaminosis, *Arch. Neurol. & Psychiat.* 39: 650 (March) 1938.

7. Zimmerman, H. M., in discussion on Lewy,⁵ p. 683.

8. Shattuck, G. C.: The Relation of Beriberi to Polyneuritis from Other Causes, *Am. J. Trop. Med.* 8: 539 (Nov.) 1928.

9. Vedder, E. B.: *Beriberi and Epidemic Dropsy*, Oxford Loese-Less Medicine 4: 273 (pt. 2) 1936.

signs of degeneration. The membranes of the cord are often congested and edematous, and the cord may appear to be abnormally soft. Scattered fibers in all tracts show the same sort of changes as are found in the peripheral nerves. Degenerative changes are found also in the cells of the anterior and of the posterior horns, and in the sympathetic ganglions as well. Marked lesions in the brain have been found also by L'Hermite (cited by Vedder). These facts have led Vedder to state that "although the symptoms of beriberi have been attributed in the past chiefly to peripheral neuritis, the condition is not a simple polyneuritis but is a degeneration of the entire nervous system as well as of other organs."

Very recently, Vedder¹⁰ has said that degenerative changes in the cord are seen particularly in the posterior columns as well as in the anterior and posterior nerve roots and that similar changes have been found in the ganglion cells of the medulla and pons as well as in the cranial nerves, particularly the phrenic and the vagus.

Of infantile beriberi, Vedder said that the degenerative changes in the nerves are usually less marked than in adult cases and that this may be because the disease is apt to be of shorter duration in infants.

According to Manson-Bahr¹¹ (p. 406) the cranial nerves above the seventh are rarely involved in beriberi but, in some cases, the laryngeal muscles are paralyzed. Laryngeal paralysis is believed to be relatively common in the infantile form of beriberi, but this symptom has been attributed by some persons to an effect of pressure on the left laryngeal nerve exerted by a dilated right auricle.^{11a}

It is interesting to note here that Brown¹² believes that in the case described by Landry,¹³ from which were derived the terms "Landry's paralysis" and "Landry's syndrome," death was due to beriberi. I agree with this view and, further, that an important group of cases which can properly be designated as Landry's paralysis or Landry's syndrome are due essentially to deficient ingestion or utilization of components of vitamin B.¹⁴

Moreover, a close relationship between Korsakoff's syndrome and beriberi seems now to have been established. At any rate, it seems to have been proved that widespread degenerative lesions of the nervous system occur in typical cases of beriberi and that such lesions have been found in nearly all parts of the nervous system, including the brain.

Korsakoff's Syndrome.—In 1890 Korsakoff¹⁵ reported six cases of psychosis that were associated with polyneuritis. In four of these cases there was no evidence of alcoholism and, in the other two cases, it was not clear that alcoholic beverages had been taken to excess. Korsakoff's syndrome, therefore, is not dependent on a background of alcoholism. No autopsy reports were included in the paper of 1890, but Korsakoff referred to two other papers published by him in Russian in 1887, which dealt respectively with "atrophic spinal

paralysis and multiple neuritis" and with "alcohol paralysis."¹⁶ He was impressed with the similarity between the conditions seen in alcoholic addicts and those not addicted to alcohol, and he expressed the view that alcohol merely facilitated the action of some other toxic substance.

Korsakoff¹⁵ (p. 693) said also in 1887 that the peripheral nerves are by far the most frequently damaged but that the spinal cord and brain frequently suffer also. It was not clear to him why such differences should occur, but he pointed out that, in alcoholic cases, cerebral pathologic changes were almost always associated with polyneuritis.

Korsakoff and Serbski¹⁷ published a detailed account of a case of polyneuritic psychosis with autopsy. They believed that alcohol played no part whatever in this case. Lesions were found in the peripheral nerves, and there was an increase of neuroglia in the columns of Goll as well as in the lateral columns in the cervical region. No lesions were found in the brain. Nevertheless, the authors believed that the symptoms in this case indicated an effect on the brain, and they said that, as in many other cases of multiple neuritis, there is reason to believe that the cause of the disorder operates on the spinal cord as well as on the brain.

Thus in Korsakoff's syndrome the lesions of the peripheral nerves, of the cord and of the brain seem to be indistinguishable from those which may be found in beriberi. I have seen a few cases of Korsakoff's syndrome in which there were cutaneous lesions suggestive of pellagra and it is well known that symptoms of polyneuritis may be associated with pellagra.

Moreover, Carmichael and Stern¹⁸ suggested tentatively that "a common factor may operate in Korsakoff's syndrome and in pellagra, or that in these conditions there may be a deficiency in an essential factor, lack of which permits toxins to attack and damage the highly specialized nerve cells of the cerebral cortex."

A close relationship between beriberi, "alcoholic polyneuritis," Korsakoff's syndrome and pellagra, with or without alcoholism, is apparent from the clinical standpoint. What, then, are the lesions found in the nervous system in pellagra?

Pellagra.—Many years ago Mott¹⁹ described widespread lesions of the nervous system in cases of pellagra. In none of his cases was there any evidence of the meningeal or perivascular cellular infiltration that is usually associated with lesions of the nervous system caused by an infecting organism. On the other hand, all the changes found were like those produced by a chronic toxemia and it was pointed out that the "combined sclerosis" of pellagra is "not unlike" that found in pernicious anemia. The pathologic changes reported by Mott were seen in all the posterior spinal ganglion cells, in all the cells of the anterior horn in varying degrees and in their homologues in the medulla and pons as well. Similar changes were observed in the Betz cells of the cortex and in the cells of Purkinje, and there was marked chromatolysis in the cells of Clarke's column. Mott characterized the lesions found as "combined sclerosis of the cord."

10. Vedder, E. B.: *The Pathology of Beriberi*, J. A. M. A. **110**: 893 (March 19) 1938.

11. Manson-Bahr, P. H.: *Manson's Tropical Diseases*, ed. 10 (revised), Baltimore, William Wood & Company, 1936.

11a. Stitt, E. R.: *The Diagnostics and Treatment of Tropical Diseases*, ed. 5 (revised), Philadelphia, P. Blakiston's Son & Co., 1929, p. 428.

12. Brown, Madeline R.: A Note on the Etiology of Landry's Acute Ascending Paralysis, *Arch. Neurol. & Psychiat.* **40**: 500 (Oct.) 1938.

13. Landry, J. B. O.: Note sur la paralysie ascendante aigue, *Gaz. hebdom. de med.* **6**: 472, 1859.

14. Shattuck, G. C.: "Landry's Paralysis" in Relation to Vitamin B Deficiency, *Internat. Clin.* **3**: 24 (Sept.) 1938.

15. Korsakoff, S. S.: Ueber eine besondere Form psychischer Störung, combinirt mit multipler Neuritis, *Archiv. f. Psychiat.* **21**: 669, 1890.

16. The references which he gives (pp. 691 and 693) are as follows: 1. A monograph entitled "Ueber die Alkohollahmung" (Russian), Moscow, 1887, p. 262. 2. "Zur Lehre von der Pathogenese der atrophischen Spinalparalyse und der multiplen Neuritis," *Arch. Psychiat.*, etc., Charkov **9**: 16, 1887.

17. Korsakoff, S. S., and Serbski, W.: Ein Fall von Polyneuritischer Psychose mit Autopsie, *Arch. f. Psychiat.* **23**: 112, 1892.

18. Carmichael, E. A., and Stern, R. O.: Korsakoff's Syndrome: Its Histopathology, *Brain* **54**: 189 (June) 1931.

19. Mott, F. W.: The Histological Changes in the Nervous System of Dr. Box's Case of Pellagra, *Brit. M. J.* **2**: 4, 1913.

Manson-Bahr¹¹ said (p. 427) that, in the cord, the middle and lower thirds of the lateral columns and the crossed pyramidal tracts are especially implicated, that the direct cerebellar tracts usually escape and that there may be wasting of the brain.

A more detailed account of the pathologic changes of the nervous system in pellagra and a review of the literature can be found in an article,²⁰ originally written by Edward Jenner Wood (date not indicated), since revised by F. R. Taylor. The following interesting points were brought out:

1. Spiller and Anderson²¹ believed that pellagra does not produce a true systemic disease of the nervous system and that degeneration is caused by some toxin that affects all parts of the cerebrospinal system.

2. Having studied thirteen cases, Wilson²² found degeneration of the posterior tracts to be more frequent than that of the lateral tracts, but the process was never confined to any system. A marked resemblance to subacute combined degeneration was noted.

3. Cotton studied a single case of Wood's which tended to confirm his belief that the lesions of pellagra are markedly similar to those found in the central neuritis of Adolf Meyer and that there is also a resemblance between them and the chromatolysis described by Marinesco.

4. A change in the ganglion cells of the sympathetic system was observed by Roaf (Report of the Egyptian Commission).

Langworthy²³ described in detail the neurologic lesions found in a woman aged 22 who died of pellagra. He said:

Accumulations of pigment were found in cells of the sensory and autonomic ganglia and in those in the spinal cord and brain-stem. The anterolateral columns of the cord were most severely involved; there was no abnormality in the posterior columns. The lesions involved particularly the spinocerebellar and corticospinal tracts. It is probable that the neurological abnormalities were of only short duration; considerable fat could be demonstrated in the lateral columns of the cord.

Similar studies by Susman²⁴ revealed complete unilateral degeneration of the dorsospinocerebellar tract in the upper thoracic region in one case, and in another case posterolateral degeneration chiefly, and slight degeneration of the direct pyramidal tracts. In one case he found perivascular pigment in the cerebrum, cerebellum and midbrain. These lesions were associated with varying degrees of degeneration of the pyramidal cells of the cortex, the Purkinje cells of the cerebellum and the ganglion cells of the midbrain.

Briefly stated, the distribution of lesions of the nervous system in pellagra is by no means uniform. Lesions of degenerative type are apt to be widespread, however, and they may be found in the peripheral nerves, the spinal cord, the medulla, the pons, the cerebellum or the cerebrum.

Although the usual distribution of the lesions in pellagra differs from that commonly seen in beriberi, the changes appear to be similar in kind. Both clinical and pathologic evidence points to a close etiologic relationship between beriberi, Korsakoff's syndrome and

pellagra. Moreover, the "central neuritis" of Adolf Meyer and "subacute combined degeneration of the cord" appear to be closely linked to pellagra.

Pernicious Anemia.—According to Minot²⁵ (p. 999) the characteristic lesion in the spinal cord in pernicious anemia is diffuse subacute combined degeneration of marginal distribution. It is usually symmetric and generally it appears first in the upper thoracic and cervical portions of the cord and in the posterior columns. The dorsal roots may be attacked early and the ventral roots later. Lesions of the peripheral nerves are found also, and the brain may show degenerative changes as well.

Woltman and Heck²⁶ listed and discussed a great variety of morbid conditions in which this syndrome had been observed. They showed the difficulty of classifying such cases until the essential etiology has been determined. In their summary they said (p. 299):

On the basis of a survey of the important available literature, it appears that this familiar and challenging picture may be brought about by chronic alcoholism, gastric carcinoma, obstruction and fistulas of the intestinal tract, pernicious anemia, so-called prepernicious anemia and scurvy. It possibly may be similarly related to pancreatitis, pellagra and hemolytic icterus, and it has been in some manner associated with amyotrophic lateral sclerosis and a number of unclassified diseases.

An important physiologic principle appears to be involved. Careful hematologic studies, gastric analysis and an investigation of the presence of Castle's intrinsic factor, if facilities are available, possibly would lead to the disclosure of some one underlying cause, probably nutritional and in the nature of a deficiency.

Pernicious anemia is listed now among the deficiency diseases. There are striking analogies between the degenerative lesions found in the nervous system in pernicious anemia, pellagra and beriberi. Subacute combined degeneration of the cord has been found in the absence of pernicious anemia, but it has also been observed in association with many disorders in which nutrition is seriously affected, such as malaria, typhoid, typhus fever, tuberculosis, alcoholism, dysentery, gastroenteric disorders, beriberi, pellagra, pernicious anemia, scurvy and sprue.

Twelve years ago, Reed and Wyckoff²⁷ pointed out a close relationship between sprue, pernicious anemia and subacute combined degeneration of the cord and reported cases to support their belief. Such a relationship has since received general acceptance.

Therefore it seems highly probable that disorders of nutrition involving deficiency of vitamins of the B complex or of unknown substances contained in liver are responsible for most of the cases of subacute combined degeneration of the cord, whether or not associated with pernicious anemia.

LESIONS OF THE CRANIAL NERVES TRACEABLE TO VITAMIN DEFICIENCY

I noted earlier that lesions of the medulla, of the vagus, of the phrenic and of other cranial nerves may occur in beriberi and that lesions of the medulla may also be found in pellagra. Many years ago, Darling²⁸

20. Wood, E. J.: Pellagra, Oxford Loose-Leaf Medicine 4: 307 (pt. 2, chap. 13) 1929; revised by F. R. Taylor.

21. Spiller, W. G., and Anderson, P. V.: Pellagra with a Report of Two Cases with Necropsy, Am. J. M. Sc. 141: 94, 1911.

22. Wilson, S. A.: The Pathology of Pellagra, Proc. Roy. Soc. Med., Lond., Neurol. Sec. 7: 31 (No. 4) 1914.

23. Langworthy, O. R.: Lesions of the Central Nervous System Characteristic of Pellagra, Brain 54: 291 (Sept.) 1931.

24. Susman, William: Morbid Anatomy and Histology of Pellagra, Tr. Roy. Soc. Trop. Med. & Hyg. 24: 23 (June) 1930.

25. Minot, G. R.: Pernicious Anemia, in Cecil, R. L.: Textbook of Medicine, ed. 4, Philadelphia, W. B. Saunders Company, 1937.

26. Woltman, H. W., and Heck, F. J.: Funicular Degeneration of the Spinal Cord Without Pernicious Anemia, Arch. Int. Med. 60: 272 (Aug.) 1937.

27. Reed, A. C., and Wyckoff, H. A.: The Common Picture of Sprue, Pernicious Anemia, and Combined Degeneration, Am. J. Trop. Med. 6: 221 (May) 1926.

28. Darling, S. T.: The Pathologic Affinities of Beriberi and Scurvy, J. A. M. A. 63: 1290 (Oct. 10) 1914.

reported finding degenerative changes in the vagus nerve in certain cases of scurvy. Moreover, he stated that the lesions of the cardiac muscle which he found in scurvy were of the "same type" as those seen in beriberi. Now that combined deficiencies are known to be common, Darling's cases might be interpreted as instances of deficiency of vitamin C combined with that of vitamin B₁.

Taylor and McDonald²⁹ suggest that the facial nerve may also become involved in severe cases of beriberi. These authors say in their conclusion (p. 243):

The etiology [of the syndrome] has not been definitely determined. The signs of infection are slight and often entirely absent. A febrile onset is inconstant. . . . The symptomatology, apart from the somewhat arbitrary coincidences of facial diplegia and general peripheral neuritis or neuronitis, is varied. No constant relationship exists between the appearance of the facial paresis and the more general signs of neuritis. . . . Pathologic changes are of the nature of a diffuse inflammation involving especially peripheral neurons, the cord and brain stem to a lesser extent and the cortex slightly if at all. The cerebrospinal fluid varies from normal to a condition characterized by a pronounced increase in total protein with slight or often no increase in the number of cells.

It appears from the foregoing that changes indicating the presence of an infectious process were present in some of the cases discussed by Taylor and McDonald but were entirely absent in others. The propriety of characterizing the changes observed in the peripheral nerves as being in the "nature of a diffuse inflammation" is open to question. With regard to this matter, Lewy⁶ (p. 222) said: "Primary inflammatory processes of the peripheral nerves are unknown. Therefore the term neuritis is erroneous and should be replaced by neuropathy." Probably, Taylor and McDonald's paper deals with cases belonging to two entirely different categories, namely (a) infectious diseases involving the central nervous system and (b) degenerative processes attributable to deficiency of vitamin B₁.

In 1931 Keefer³⁰ listed among the clinical features of vitamin B deficiency aducens palsy, facial palsy and retrobulbar neuritis.

Reviewing the subject of nutritional diseases of the eye, Benedict and Wagener³¹ listed among them retrobulbar neuritis, optic neuritis and paralysis of the ocular muscles. The same subject was discussed by Fine and Lachman,³² and Moore³³ pointed out that retrobulbar neuritis followed by more or less optic atrophy is common in pellagra and that this fact has not been fully appreciated. Cohen³⁴ has called attention to the fact that visual disturbances and optic atrophy may precede other neurologic and blood changes in pernicious anemia and that the lesions yield to liver extract when treated early.

Carroll³⁵ reported ten cases of "alcohol" amblyopia which occurred in patients who had pellagra or polynuritis or both. All were heavy drinkers. In every

case, he said, the diet had been inadequate. In the following year Carroll³⁶ stated that nutrition apparently plays an important role in tobacco-alcohol amblyopia and reported on a small series of cases in which satisfactory improvement occurred on an adequate diet high in vitamin B without diminishing the amount of alcohol previously taken or the tobacco used.

Laryngeal paralysis has already been mentioned as occurring occasionally in beriberi, but the significance of this symptom is uncertain.^{11a}

A possible relationship between "chronic progressive deafness" and deficiency of vitamin B₂ has been suggested by Selfridge.³⁷

The contributions of the authors quoted serve to emphasize the fact that lesions of various cranial nerves may be associated with a number of different deficiency syndromes.

LESIONS OF THE BRAIN

Without undertaking a discussion in detail of the lesions of the cerebrum which accompany known deficiency syndromes, it may nevertheless be worth while to point out that cerebral lesions of the "degenerative type" have been described for beriberi, pellagra, Korsakoff's syndrome and pernicious anemia. Moreover, cerebral symptoms and psychic disorders may be associated with any of these diseases.

Various types of changes in the brain in cases of cachexia associated with gastrointestinal infection have been described by Alexander and Wu.³⁸

It is well known that the type of psychic disorder which commonly appears in the later stages of pellagra is, in some cases, the presenting symptom. Because this type of mental disorder is not very clearly definable, the true nature of such cases may be obscure until other more characteristic lesions appear. Therefore, is it not reasonable to infer that there are cases in which the characteristic lesions of pellagra or of some other deficiency syndrome do not develop and which, nevertheless, are caused essentially by some disorder of nutrition? If this inference is correct, the psychiatrist may ultimately come to believe that inadequate nutrition plays a far more important role in his field than has yet been assigned to it. At this point the fact requires emphasis that deficiency syndromes are not necessarily accompanied by emaciation. Certain acute cases of beriberi and of pellagra bear witness to this truth.

SUMMARY

There seems to be adequate ground for the following inferences:

1. The lesions of the nervous system which are common in beriberi, pellagra, Korsakoff's syndrome and pernicious anemia, as well as those found in many cases of combined degeneration of the cord, in Landry's paralysis and in polynuritis associated with a great variety of morbid conditions, are traceable to deficiency of diet or to conditions that interfere with utilization of factors contained in food which has been ingested.

2. The morbid processes so produced in the nervous system are similar in character and are often widespread.

29. Taylor, E. W., and McDonald, C. A.: The Syndrome of Polynuritis with Facial Diplegia. *Tr. Am. Neurol. A.*, 1931, p. 210; *Arch. Neurol. & Psychiat.*, 27:79 (Jan.) 1932.

30. Keefer, C. S.: Some Clinical Aspects of Deficiency Diseases, *New England J. Med.*, 205:1086 (Dec. 3) 1931.

31. Benedict, W. L., and Wagener, H. P.: Nutritional Diseases and the Eye: The Role of Vitamin B, *Am. J. M. Sc.*, 192:296 (Aug.) 1936.

32. Fine, Max, and Lachman, G. S.: Retrobulbar Neuritis in Pellagra, *Am. J. Ophthalm.*, 20:708 (July) 1937.

33. Moore, D. G. F.: Retrobulbar Neuritis cum Avitaminosis, etc., *West African M. J.*, 9:35 (June) 1937; *abstr. Trop. Dis. Bull.*, 35:72, 1937.

34. Cohen, Henry: Optic Atrophy as Presenting Sign in Pernicious Anemia, *Lancet*, 2:1202 (Nov. 21) 1936.

35. Carroll, F. D.: "Alcohol" Amblyopia, Pellagra, Polynuritis: Report of Ten Cases, *Arch. Ophthalm.*, 16:919 (Dec.) 1936.

36. Carroll, F. D.: Recovery from Tobacco-Alcohol Amblyopia with Continuance of Tobacco and Alcohol, *Arch. Ophthalm.*, 18:176 (July) 1937; *Importance of Diet in the Etiology and Treatment of Tobacco-Alcohol Amblyopia*, *ibid.*, 18:948 (Dec.) 1937.

37. Selfridge, G. L.: Chronic Progressive Deafness from Nutritional Standpoint: Preliminary Report, *Ann. Otol., Rhin. & Laryng.*, 46:875 (Dec.) 1937.

38. Alexander, Leo, and Wu, T. T.: Symptomatic Involvement of the Nervous System in Different Forms of Dysentery, *Chinese M. J.*, 48:1 (Jan.) 1934; Cerebral Changes in Gastrointestinal Infections with Terminal Cachexia, *Arch. Neurol. & Psychiat.*, 33:72 (Jan.) 1935.

3. The presenting symptoms may be traceable to almost any part of the nervous system. Therefore a great variety of clinical syndromes may result from deficiency states.

4. Neurologic lesions caused essentially by deficiency are usually traceable to lack of a part or parts of the vitamin B complex or of something contained in liver.

5. Many neurologic syndromes which have not yet been attributed to deficiency are likely to be so regarded in the future. Still other conditions within the field of psychiatry may, perhaps, be added to the list.

6. Any patient having neurologic or psychiatric symptoms such as are known to exist in deficiency states should be adequately treated in the early stages of the disorder when complete recovery of the nervous system may still be possible.

NOTE.—In order not to make this paper too long, I have omitted consideration of some important papers on the treatment of various neurologic lesions in man which have improved markedly after treatment with liver extract or with vitamin preparations.

Experimental work on animals has also given important results, but the response of animals to vitamin deficiencies differs in some respects from that of man.

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THE RELATION OF HUMAN ENCEPHALITIS TO ENCEPHALOMYELITIS IN HORSES

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In 1931 Meyer, Haring and Howitt¹ reported the discovery of a virus as the cause of an epizootic of encephalomyelitis among horses and mules in the San Joaquin Valley of California during the summer of 1930. Since that time the disease has occurred in several Western and Midwestern states. Similar epizootics have occurred during the past seventy years, especially in the West Central states, but have been confused with other equine diseases. In 1933 the disease appeared in Maryland, Delaware, Virginia and New Jersey. In this year Ten Broeck and Merrill² and Giltner and Shahan³ reported the isolation of an eastern strain of virus of equine encephalomyelitis which, though similar to the western strain, differed serologically. The disease in the horse was more acute and fatal, and the virus appeared to be more virulent for laboratory animals.

The viruses of equine encephalomyelitis differ immunologically from the viruses of lymphocytic choriomeningitis, the St. Louis type of encephalitis, Borna disease, vesicular stomatitis and poliomyelitis.⁴

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1. Meyer, K. F.; Haring, C. M., and Howitt, B. F.: The Etiology of Epizootic Encephalomyelitis of Horses in the San Joaquin Valley 1930, *Science* 74: 227 (Aug. 28) 1931.

2. TenBroeck, Carl, and Merrill, M. H.: A Serological Difference Between Eastern and Western Equine Encephalomyelitis Virus, *Proc. Soc. Exper. Biol. & Med.* 31: 217 (Nov.) 1933.

3. Giltner, L. T., and Shahan, M. S.: The 1933 Outbreak of Equine Encephalomyelitis in the Eastern States, *North Am. Vet.* 14: 25 (Nov.) 1933.

4. Howitt, Beatrice F.: The Complement Fixation Reaction in Experimental Equine Encephalomyelitis, Lymphocytic Choriomeningitis, and the St. Louis Type of Encephalitis, *J. Immunol.* 32: 235 (Sept.) 1937; Cross Immunization Experiments with Poliomyelitis Virus and That of Encephalomyelitis in Horses, *Proc. Soc. Exper. Biol. & Med.* 29: 118 (Nov.) 1931. Cox, H. R., and Fite, G. L.: Serological Distinction Between the Virus of Encephalitis in St. Louis, 1933 Equine Encephalomyelitis and Vesicular Stomatitis, *ibid.* 31: 499 (Jan.) 1934.

Present epidemiologic and experimental evidence points to the spread of infection by an insect vector rather than by contact. Experimentally mosquitoes can be infected and transmit the virus to laboratory animals and horses. *Aedes aegypti*, *A. sollicitans*, *A. nigromaculis*, *A. dorsalis*, *A. albopictus* Skuze, *A. vexans* and *A. taeniorhynchus* can transmit the western strain, *A. cantator* and *A. sollicitans* the eastern strain.⁵ To date no one has found infected mosquitoes in localities where equine encephalomyelitis is prevalent.

Meyer⁶ in 1932 suggested the possibility of human infection. He briefly reported three cases of encephalitis occurring in men closely associated with horses having encephalomyelitis. One, a ranch hand, died in July 1931; microscopic examination of the central nervous system showed manifestations resembling those in horses. A nonfatal case occurred in September 1931. Meyer was unable to demonstrate neutralization of the virus of equine encephalomyelitis by blood serum obtained during convalescence. A third case with recovery occurred in a veterinarian in July 1932. An attempt to isolate virus from the blood and spinal fluid was unsuccessful. This patient was given serum intramuscularly from a hyperimmunized horse. He presented these cases with the suggestion that in the future the central nervous system of patients who died of atypical human encephalitis be investigated for the presence of the virus of equine encephalomyelitis.

Equine encephalitis has been definitely known to occur in Minnesota since the summer of 1934 and was very prevalent in Minnesota during the summer of 1937. Of 737,000 horses in Minnesota, 41,159 were affected and 9,200 of these died.⁷ The western strain of encephalomyelitis virus is the only one that has been isolated in Minnesota.⁸ Of the mosquitoes shown to transmit the western strain experimentally, three occur in Minnesota: *A. vexans*, *A. nigromaculis* and *A. dorsalis*.⁹ *A. vexans* is one of the most common and widespread mosquitoes in Minnesota. It has been found as late as October. The other two mosquitoes are found in small numbers only. *A. dorsalis* has been found as late as July 27 and *A. nigromaculis* as late as August 4, but their times of occurrence have been incompletely studied.

During the last week of August and the first two weeks of September 1937 six cases of human encephalitis were reported from a county in northwestern Minnesota.¹⁰ All were in farmers, five of whom had had contact with sick horses. The sixth patient (C. S.)

5. Kelser, R. A.: Mosquitoes as Vector of the Virus of Equine Encephalomyelitis, *J. Am. Vet. M. A.* 82: 767 (May) 1933; Transmission of the Viruses of Equine Encephalomyelitis by *Aedes Taeniorhynchus*, *Science* 85: 178 (Feb. 12) 1937. Merrill, M. H.; Lacaille, C. W., and Ten Broeck, Carl: Mosquito Transmission of Equine Encephalomyelitis, *ibid.* 80: 251 (Sept. 14) 1934. Madsen, D. E., and Knowlton, G. F.: Mosquito Transmission of Equine Encephalomyelitis, *J. Am. Vet. M. A.* 86: 662, 1935. Simmons, J. S.; Reynolds, F. H. K., and Cornell, V. H.: Transmission of the Virus of Equine Encephalomyelitis Through *Aedes Albopictus* Skuze, *Am. J. Trop. Med.* 16: 289 (May) 1936.

6. Meyer, K. F.: A Summary of Recent Studies in Equine Encephalomyelitis, *Ann. Int. Med.* 6: 645 (Nov.) 1932; Equine Encephalomyelitis, *North Am. Vet.* 14: 30 (June) 1933.

7. Cotton, C. E., executive secretary Minnesota State Live Stock Sanitary Board: Personal communication to the authors.

8. Howitt, Beatrice F.: An Immunological Study in Laboratory Animals of Thirteen Different Strains of Equine Encephalomyelitis, *J. Immunol.* 29: 319 (Oct.) 1935. Fenstermacher, R., assistant professor of veterinary medicine, University of Minnesota: Personal communication to the authors.

9. Owen, W. B.: The Mosquitoes of Minnesota with Special Reference to Their Biology, Technical Bulletin 126, University of Minnesota Agricultural Experiment Station, November 1937.

10. In eleven counties in northwestern Minnesota, including the district in which human cases occurred, of 14,929 horses 3,826 horses were sick and 904 died. *A. vexans* and *A. dorsalis* have been found in this area.

had had no contact with sick horses at the time of onset of his illness. He had run a tractor on a farm in North Dakota not far from the Minnesota border. There was much equine encephalomyelitis in this locality. Two of the men had had contact with each other and with the same sick horses while threshing. The onset of their illnesses were August 29 and September 10. The others had not had any contact with one another or with any sick person. No other case occurred in the families of these six men.

All six patients were men ranging in age from 22 to 51. The onset of the disease was sudden with headache, nausea, vomiting, dizziness, drowsiness and fever. Two of the men died after illnesses of four and five days. In three cases the acute illness lasted about a week. In the sixth case (C. S.) the acute illness lasted about three weeks. An autopsy was done in one instance.

On microscopic examination of the central nervous system the chief pathologic changes were found in the gray matter of the spinal cord. On hematoxylin-eosin stain, about one third of the nerve cells in the cervical segment appeared to be affected. The cells were in various stages of disintegration. In the main they showed swelling and chromatolysis. Occasionally there was pyknosis and rarely, slight evidence of neuronophagia. Scattered rather densely throughout the gray matter were nests of lymphocytes, consisting of from five to 100 cells. There were no definite hemorrhages. The white matter of the cord showed a mild degree of lymphocytic perivascular cuffing. Rarely there could be seen a small nest of glial cells numbering from five to twenty-five. The meninges showed a moderate degree of lymphocytic infiltration. Sections of the brain on hematoxylin-eosin stain showed minimal changes, which consisted mainly of a moderate degree of lymphocytic cuffing. There was no definite evidence of nerve cell degeneration and there were no distinct hemorrhages.

Blood was collected from three of the patients who recovered during January 1938 and the serums were forwarded to Dr. Carl Ten Broeck of the Rockefeller Institute for Medical Research. Under date of April 21, 1938, Dr. Ten Broeck reported that he had demonstrated neutralization of the western strain of equine encephalomyelitis virus by the serum of one of the patients (C. S.): Blood was collected again in May from this patient and neutralization was again demonstrated by Dr. Ten Broeck.

During the latter part of August and the early part of September of this year attacks of what appear to be a similar illness have occurred. Most of the patients have had no contact with sick horses. The majority live on farms or in small towns. Blood serums from patients have been collected for studies of the virus.

SUMMARY

In the summer of 1937 six cases of encephalitis occurred among farmers in localities where equine encephalomyelitis was prevalent. The blood serum of one of three patients was shown to neutralize the western strain of equine encephalomyelitis by Dr. Ten Broeck of the Rockefeller Institute for Medical Research.

As far as is known, this is the first time that neutralization of the virus of equine encephalomyelitis by human serum has been found.

HUMAN ENCEPHALITIS

EIGHT FATAL CASES, WITH FOUR DUE TO THE
VIRUS OF EQUINE ENCEPHALOMYELITIS

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During the first week in August 1938 an outbreak of equine encephalomyelitis causing the death of more than 200 horses occurred in southeastern Massachusetts and Rhode Island. August 12 a girl aged 12 years was referred to the Haynes Memorial Hospital with a diagnosis of epidemic cerebrospinal meningitis. On admission a provisional diagnosis of encephalitis was made. Seven hours after admission the patient suddenly died. At autopsy the diagnosis of encephalitis was confirmed. No virus studies were made on the brain. Seventeen days later, August 29, a boy aged 13 years was admitted from the same city, presenting much the same clinical picture. In view of the existing epidemic of equine encephalomyelitis in the same area, the spinal fluid obtained from the lumbar puncture was injected into mice but the results were inconclusive. Death occurred twenty hours after entry. Unfortunately permission for an autopsy was not granted.

Similar cases continued to appear and were admitted to other hospitals, twenty-four cases in all to date. Six more patients with encephalitis were admitted to the Haynes Memorial Hospital up to September 17, all of whom died, and all were examined post mortem. Specimens of brain tissue collected in glycerin were sent to Dr. Fothergill at the Boston Children's Hospital and through the state department of health to Dr. L. T. Webster at the Rockefeller Institute. September 13 Dr. Fothergill found the virus of the eastern strain of equine encephalomyelitis in a patient who had died at the Children's Hospital, the report of which was published in the *New England Journal of Medicine*.¹ September 15 Dr. Webster reported that he had recovered this same strain of virus from three of our patients and later from a fourth. He has since published his observations on these and four other cases.²

The high mortality rate among the horses has been paralleled in these human cases. Furthermore, it is of epidemiologic interest that the peak of the human cases of encephalitis in this area appears to have coincided with the peak of the epidemic in the horses. None of our patients came in contact with a horse but they all had been living within the area where horses had been stricken. Simmons³ has recently discussed the role of mosquitoes in the transmission of the virus among horses. The fact that in this region seven established cases of this equine type should have occurred in human beings during a period when mosquitoes were unusually

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Dr. LeR. D. Fothergill and Dr. Sidney Farber of the Children's Hospital, Dr. L. T. Webster of the Rockefeller Institute and Dr. R. F. Feemster of the Massachusetts State Department of Health gave their cooperation and assistance in the study of these cases.

1. Fothergill, L. D.; Dingle, J. H.; Farber, Sidney, and Connerley, M. L.: Human Encephalitis Caused by the Virus of the Eastern Variety of Equine Encephalomyelitis, *New England J. Med.* **219**: 411 (Sept. 22) 1938.

2. Webster, L. T., and Wright, F. H.: Recovery of Eastern Equine Encephalomyelitis Virus from Brain Tissue of Human Cases of Encephalitis in Massachusetts, *Science* **88**: 305 (Sept. 30) 1938.

3. Simmons, J. S.: The United States Army's War in the Air Against the Mosquito-Borne Diseases, *Am. J. M. Sc.* **196**: 165-166 (Aug.) 1938.

prevalent prompts us to report the clinical aspects and pathologic changes found in eight fatal cases of encephalitis from this area which came under our observation at the Haynes Memorial Hospital, in four of which this virulent equine strain has been found.

The clinical aspect of these Massachusetts cases differs from epidemic human encephalitis in the much greater severity of the symptoms and the high mortality. In the St. Louis epidemic⁴ the incidence and the mortality rate were definitely greater in older persons, yet it appears from the few reported human cases of encephalitis in this minor epidemic that children are more susceptible than adults. The question arises as to whether there have been milder cases in which recovery has occurred. That is a problem outside the scope of this paper. Of course a great number of mild cases of encephalitis go unrecognized as such. This is certainly true of the milder forms of encephalitis accompanying chickenpox, the meningo-encephalitis of mumps and measles, and even encephalitis lethargica. It seems, therefore, reasonable to suppose that some cases have passed unrecognized, a factor which if known would modify the case rate mortality. However, it is of significance that very few horses recovered and that the only human subjects as yet positively known to have harbored this virulent strain of equine virus are dead.

The variation in the onset is particularly striking. The onset in the infants was abrupt; in the three older children and the adult the period of invasion lasted several days before the signs of encephalitis set in. Patient 6 had complained of pain in the back of the legs for two weeks before admission to the hospital. In cases 2 and 8 there was a period of remission with definite improvement in the symptoms. In all the cases there seemed to be an abruptness in the onset of the severer symptoms in the form of dizziness, vomiting, droopiness, twitching of the muscles or convulsions. Aphasia, diplopia and palsies signified cerebral insults. Hyperpyrexia was constant. All the symptoms proceeded to a lethargy and coma. The deaths were all due to encephalitis, and the terminal evidence of myocardial insufficiency and pulmonary symptoms contributed little or not at all as actual causes of death. This again is in striking contrast to the St. Louis epidemic, where not more than 10 per cent of the deaths were attributable to uncomplicated epidemic encephalitis.⁴

This statement requires qualification because a remarkable complication did exist in three of the four infants (cases 4, 5 and 7), namely whooping cough; in each one a diagnosis from the cough had been made three weeks before the onset of the symptoms of encephalitis, prior to which they had shown an improvement in the cough. All three of these were referred to the hospital as having "whooping cough with convulsions." However, they all showed signs and symptoms of a severe encephalitis, which was confirmed by the appearance of the brain at autopsy and by subsequent microscopic appearances, all of which were entirely out of keeping with those seen in whooping cough. In two of these cases the virus of the eastern strain of equine encephalomyelitis was found in the brain tissue. It was the severe type of encephalitis resembling that observed in the other cases and the appearance of the brain at autopsy that prompted us to suspect that we were dealing with something more than the cerebral complications of whooping cough.

A contagious disease service receives numerous cases of convulsions occurring in the course of whooping cough. Convulsions occurred in 2.3 per cent of cases of pertussis at the Metropolitan Asylums Board Hospitals in London,⁵ 2.2 per cent at the Herman Kiefer Hospital in Detroit⁶ and in 7.4 per cent of our cases at the Haynes Memorial Hospital. Just what the percentage of this complication is in this disease remains unknown, because only comparatively few patients with uncomplicated pertussis are hospitalized. The spinal fluid in pertussis without neurologic complications is normal.⁷ Ordinarily when convulsions occur in this disease the spinal fluid shows only a moderate increase in the number of cells, from 10 to 100, although an accompanying meningitis shows a turbid fluid with a cell count in the thousands.⁸ The white blood count may often rise to over 100,000 in severe whooping cough in infants, and the peak is reached when convulsions take place. A relative lymphocytosis prevails unless a mixed infection occurs with bronchopneumonia or otitis media.

Encephalitis⁹ is a very rare complication of whooping cough and, if recovery takes place, is apt to leave a wake of mental disorders. Esche¹⁰ reports only one case among 172 cerebral complications. Sears¹¹ has suggested that a special neurotropic virus might be stimulated to activity by the pertussis, as has been considered in the case of the encephalitis following acute exanthematous diseases and vaccination, in which this complication also appears after the acute phase has passed. Furthermore, Sears points out that the encephalitis of whooping cough cannot be differentiated from that which occurs in the course of other acute infections. Many writers on the subject are coming more and more to the opinion that a mechanical factor alone does not account for the many neurologic conditions which can take place in pertussis.

Reports are extremely rare of the clinical manifestations of encephalitis in the course of pertussis. In one case reported from Buenos Aires¹² the cell count of the spinal fluid was 70 and all were polymorphonuclear leukocytes. In a case reported from Germany¹³ in which recovery occurred the white count was 61,000 with 71 per cent lymphocytes, while the spinal fluid was clear with only 12 cells.

It is therefore reasonable to assume from the severity of the clinical course, from the gross appearance at autopsy and from the histologic specimens as well as from the finding of the virus in the brains of two of these infants that all three suffering from whooping cough died of an encephalitis due to the virus of the eastern strain of equine encephalomyelitis.

REPORT OF CASES

CASE 1.—A girl aged 12 years, from Brockton, had had chickenpox and measles. The tonsils and adenoids had been removed. Otherwise the patient had always been well. The

5. Rolleston, J. D.: *Acute Infectious Diseases*, New York, Physicians & Surgeons Book Company, 1925, p. 115.

6. Gordon, J. E.: *Herman Kiefer Hospital Five Year Report*, 1927-1931, p. 377.

7. Magnussoo, J. H.: *Findings of Cerebrospinal Fluid in Pertussis Without Neurological Complications*, *Acta paediat.* 20:222, 1937.

8. Reiche, F.: *Keuchhustenkrämpfe*, *Ztschr. f. Kinderh.* 25:34, 1930.

9. Mikulowski, W.: *Ueber encephalitische Erkrankungen bei Keuchhusten*, *Acta paediat.* 9:454, 1930. Eley, R. C.: *Neurological Complications of Whooping Cough*, *New England J. Med.* 203:165 (July 24) 1930.

10. Comby, Jules, and Comby, Marie-Thérèse: *L'encephalite aigue au cours de la coqueluche*, *Arch. de med. d. enf.* 38:597 (Oct.) 1935.

11. Esche, C.: *Pathogenese der cerebralen Komplikationen des Keuchhustens*, *Monatschr. f. Kinderh.* 61:459, 1935.

12. Sears, W. G.: *Nervous Complications of Whooping Cough*, *Brit. J. Child. Dis.* 26:191 (July-Sept.) 1929.

13. Mendilabarzu, J. R., and Coleccchia, J. M.: *Encefalopatia coqueluchosa*, *Semana med.* 1:29 (Jan. 7) 1937.

14. Wiesner, Bernhard: *Eine wenig häufige Verlaufsform der Keuchhusten-Encephalitis*, *München. med. Wchnschr.* 82:786 (May 16) 1935.

4. Barr, D. P.: *The Encephalitis Epidemic in St. Louis*, *Ann. Int. Med.* 8:37 (July) 1934.

father died of rheumatic fever with endocarditis. She had a sister with rheumatic heart disease.

Onset occurred Aug. 2, 1938, with severe frontal headache, nausea without vomiting, and increasing drowsiness. August 9 there had been such an improvement in these symptoms that she went to the theater. That evening these symptoms reappeared and grew gradually more severe. On the 11th vomiting began and she complained of pain in the back of the neck. The following day there was intermittent twitching of both shoulders. She was admitted to the Brockton Hospital with pain in the right ear, tinnitus, dizziness, rigidity of neck and nystagmus of the right eye. The temperature was 104.6 F., the pulse 130 and the respiratory rate 25. Lumbar puncture revealed a hazy cerebrospinal fluid with an initial pressure of 320. The cell count was 920, mostly polymorphonuclear leukocytes with a few red cells. Prontosil (the disodium salt of 4-sulfamidophenyl-2'-azo-7'-acetyl-amino-1'-hydroxynaphthalene-3', 6' disulfonic acid) was given intramuscularly.

August 12 she was referred to the Haynes Memorial Hospital with a diagnosis of epidemic cerebrospinal meningitis. There was deep stupor on admission. The temperature was 102.6 F., pulse 100 and respiratory rate 26. The pupils were equal and moderately dilated, with a sluggish reaction to light. There was no nystagmus or strabismus. Muscular twitchings were present over the mandibles. There was involuntary urination (prontosil-colored urine). The lungs were normal. The size and position of the heart were normal but there was a gallop rhythm with a systolic murmur at the apex transmitted to the axilla. The abdomen was normal. Reflex of the biceps and triceps and the knee jerk were absent. The Kernig and Babinski reflexes were bilateral. The hemoglobin content was 90 per cent. The white blood cells numbered 19,050, with 90 per cent polymorphonuclear leukocytes. Examination of the cerebrospinal fluid revealed a normal pressure, a cell count of 1,500, polymorphonuclear leukocytes predominating; tubercle bacilli were not present. The patient suddenly became cyanotic and died at 8:15 p. m.

The family history and cardiac murmur bring up consideration of cerebral embolus, but at autopsy the heart was entirely normal. Furthermore, there was nothing sudden about the onset. Clinically this was a remittent type of encephalitis, the second phase being very severe and ending abruptly with simultaneous cessation of respiration and heart beat. No virus studies were made. Death occurred on the tenth day of the disease.

CASE 2.—A boy aged 13 years, from Brockton, with a negative past history, complained of frontal headache, dizziness and weakness August 22, which caused him to remain in bed. The following two days he was up and about, with intermittent headache, anorexia and backache. August 25 he stayed in bed because of weakness, headache, backache and pains in the legs. On the 27th there were drowsiness and photophobia. On the 28th the patient vomited and had a convulsion; he was taken to the Brockton Hospital, where he showed twitching of a generalized nature, rigidity of the neck with hyperextension and stupor, from which he could be aroused to answer questions. The pupils were equal and reacted to light. The fundi showed clear disks. The tendon reflexes in the arms were absent, in the legs they were diminished. The Kernig and Babinski reflexes were marked on both sides. Examination of the urine was essentially negative. The hemoglobin content was 100 per cent; red blood cells numbered 5,280,000, white blood cells 18,400; polymorphonuclears 81 per cent, lymphocytes 14 per cent, monocytes 5 per cent, platelets normal. Lumbar puncture revealed: initial pressure 250; dynamics normal; cerebrospinal fluid hazy, with a cell count of 990, mostly polymorphonuclears, sugar 83 mg. per hundred cubic centimeters and globulin positive. Two hours after entry facial palsy developed on the left side. He was referred to the Haynes Memorial Hospital August 29 with a diagnosis of poliomyelitis, encephalitis or lymphocytic meningitis. On admission the temperature was 104.6 F., the pulse rate 110 and the respiration shallow, at the rate of 36. Hyperesthesia was present on the anterior half of the scalp. The pupils were equal and reacted to light. There was slight ptosis of the left

eyelid with left facial paralysis. The jaws were firmly set. There was marked rigidity of the neck with hyperextension and marked twitchings of the arms and shoulders. The lungs were normal. The size and position of the heart were normal; there was a marked systolic murmur over the precordia, loudest at the base. The abdomen was normal. Tendon reflexes of the arms and legs were absent. Ankle clonus was absent. The Kernig and Babinski reflexes were present on both sides. Examinations of the blood and spinal fluid gave essentially the same results as those reported from the Brockton Hospital. Four grains (0.26 Gm.) of soluble phenobarbital was given intravenously. August 30 at 7:30 a. m. a convulsion occurred, with rigidity and opisthotonos lasting several minutes. The injection of soluble phenobarbital was repeated and lumbar puncture was done again. At 9:30 a. m. the patient had a convulsion. Fifty cc. of 25 per cent dextrose was given intravenously. Coarse moist rales were heard throughout. At 11 o'clock there was less rigidity of the jaws and neck. Cyanosis was evident. At 1:15 p. m. the mouth was filled with frothy mucus. At 5 o'clock the patient was completely relaxed. Shallow rapid respiration set in and the patient died at 8:10 p. m.

This was a remittent type of encephalitis with facial paralysis, convulsions and opisthotonos. Virus studies were made on the spinal fluid with inconclusive results to date. Death occurred on the eighth day of disease; permission for autopsy was not given.

CASE 3.—A girl aged 13 months, who lived in Abington, had the onset of this illness August 29 with restlessness, irritability, anorexia, drowsiness, fever and vomiting. Convulsions occurred at 2 and 2:30 p. m. She was taken to the Moore Hospital in Brockton, where she was found to have rigidity of the neck and flaccid paralysis of the right arm and leg. On lumbar puncture the cerebrospinal fluid showed 1,500 cells, all lymphocytes. She had numerous mosquito bites. She was transferred to Haynes Memorial August 30 at 6:30 p. m. On admission the rectal temperature was 104.4 F., pulse rate 162 and respiratory rate 42. There was a puffy appearance about the eyes and of the hands. She did not resist examination but took fluid with difficulty. Examination of the nose and throat was negative. The lungs, heart and abdomen were normal. The pupils were equal and reacted to light. There was no evidence of paralysis of the cranial nerves or of the extremities. There was moderate rigidity of the neck. The tendon reflexes of the arms and legs were normal. The abdominal reflex was absent on the right. The Kernig and Babinski reflexes and ankle clonus were absent. The hemoglobin content was 85 per cent. Red blood cells numbered 4,400,000, white blood cells 27,250, with polymorphonuclear leukocytes 84 per cent and lymphocytes 13 per cent. The cerebrospinal fluid had the appearance of ground glass; it had a pressure of 240, and 525 cells. Polymorphonuclear leukocytes and lymphocytes were equal. August 31 muscular twitchings developed over the entire left side. The patient became lethargic. September 1 lumbar puncture showed a pressure of 135, and 660 cells with lymphocytes predominating. Vomiting and convulsions set in. September 2 the rectal temperature was 107 F., the pulse rate 160 and the respiratory rate 90. Convulsions continued, with general rigidity. Cistern puncture showed the cerebrospinal fluid clear, a pressure of 108 and cells 252, mostly lymphocytes. September 3 the rectal temperature was 103 F.; the patient was comatose and there was muscular twitching. Small petechial spots appeared on the anterior and posterior surfaces of both arms. The temperature, pulse rate and respiratory rate fell from here on. September 4 the white blood cells numbered 8,200, polymorphonuclear leukocytes 20 per cent, lymphocytes 75 per cent and endothelial phagocytes 5 per cent. September 6 the comatose condition continued with complete relaxation. September 7 lumbar puncture revealed a cell count of 150, mostly polymorphonuclears. There were fine moist rales at both bases. The patient died September 9. Intravenous dextrose and saline clyses were given throughout, along with feeding by nasal tube during the coma.

This was a case of encephalitis with convulsions on the day of onset, growing progressively worse, with temporary paralyses, muscular twitchings and rigidity

merging into relaxation. On the fifth day the rectal temperature reached 107 F., falling gradually to normal before death on the twelfth day. Results of studies on the virus showed that it was positive for the equine strain.

CASE 4.—A boy aged 2 years 10 months had had measles at 3 months and chickenpox at 1 year. He had not been vaccinated. He lived in Plainfield and two days before the onset of the present illness was in Randolph and Brockton. He had had whooping cough for three weeks and was said to have been improving as regards frequency and severity of paroxysms. At the onset September 1 at noon he had a convulsion, which occurred when he was asleep. Dr. Farley found no meningeal signs. A second convulsion occurred at 3 p. m., after which there was rigidity of the neck and spine with generalized muscular twitchings and irregular respirations. He was admitted to the Haynes Memorial Hospital at 6 o'clock. He was well developed and well nourished. The rectal temperature was 101.2 F., the pulse rate 160 and respiratory rate 32. He was stuporous and rigid and could not be aroused. There were drooling and persistent twitchings about the mouth, rolling of the eyeballs and occasional convulsive movements of the left arm and leg. The teeth were clenched. The fauces was normal except for post nasal mucus. The left tympanum was injected. The skin was clear. There was no nasal discharge. The pupils were dilated and equal and reacted sluggishly to light; the eyeballs oscillated. The cervical glands were slightly palpable on both sides. The lungs, heart and abdomen were normal. There was rigidity of the neck and spine. The biceps reflex on the left side, the knee jerk reflex on both sides and the abdominal reflexes were absent. The cremasteric reflex was present but was sluggish on the right. The Brudzinski sign was present. The Kernig and Babinski signs and ankle clonus were absent. There was no evidence of paralysis. The white blood cells numbered 65,900; polymorphonuclear leukocytes 53 per cent, lymphocytes 43 per cent. On lumbar puncture pressure of the cerebrospinal fluid was 210 and showed cells 200, lymphocytes predominating, sugar 143 and globulin 95. There were infrequent paroxysms of coughing with whoop. September 2, the temperature was 104.4 F., the pulse rate 160 and respiratory rate 60. Convulsions continued, beginning in the right arm and then the right leg, with opisthotonos and cyanosis and cessation of respirations. The patient became comatose. The cremasteric reflex was absent. Lumbar puncture gave the same results. September 3 the temperature was 104.6 F., the pulse rate 160 and the respiratory rate 28, of Cheyne-Stokes type and stertorous. The patient died at 8 p. m. Treatment consisted of $\frac{1}{32}$ grain (0.002 Gm.) of morphine, dextrose intravenously and saline solution by hypodermoclysis, and repeated artificial respiration.

In this case encephalitis was ushered in by convulsions three weeks after the onset of whooping cough. Muscular twitchings, opisthotonos, rigidity, cyanosis and respiratory failure occurred. Death transpired on the third day of the disease. The virus was positive for the equine strain.

CASE 5.—A girl aged 13 months, who lived in Marlboro, had a negative past history. She had had a cough for three weeks, which was diagnosed by a local physician as whooping cough; it was mild and was improving. Except for the cough she was well. The onset of the present acute condition took place September 1 with a temperature of 105 F., projectile vomiting and diarrhea, and she was seen again by her physician. On the morning of September 3 she became lethargic and convulsive movements of the face and arms developed. She was referred from the Children's Hospital because of whooping cough and admitted to the Haynes Memorial Hospital at 3 p. m. The rectal temperature was 102.6 F., the heart rate 180, and the respiratory rate 28. The patient was well developed and well nourished and had moderate rigidity of the neck and spine; the head was turned persistently to the left, and the eyes were wide open and rolled upward and to the left with lateral nystagmus and diminished wink reflex. The pupils were equal and reacted

to light. There was occasional muscular twitching of the limbs and about the mouth. The right tympanum was slightly injected. The teeth were clenched. The gag reflex was present. The pharynx was injected and the tonsils were slightly enlarged. There was coughing without whoop. There was slight cervical adenopathy on the left. The lungs, heart and abdomen were normal. The arms were flexed and spastic. The biceps and triceps reflexes were normal. The legs were extended, rigid and spastic. The knee jerks were increased, on the right more so than on the left. The Kernig sign was present on both sides and the Babinski sign on the right; ankle clonus was absent. Tâche cérébrale was absent. The white blood cell count was 50,900, with polymorphonuclear leukocytes 83 per cent. On lumbar puncture the cerebrospinal fluid had a ground glass appearance, with a pressure of 240, cell count of 710 with polymorphonuclears 56 per cent. Globulin and sugar were normal. During the evening convulsions lasted one hour; the face, arms and legs twitched constantly, followed by shallow respirations and complete relaxation. The patient vomited. The rectal temperature rose to 108.5 F. and she died with respiratory failure at 1:35 p. m. September 4.

In this case encephalitis was ushered in by projectile vomiting and diarrhea, occurring three weeks after the onset of whooping cough. The diarrhea stopped after the first day. Convulsions, muscular twitchings and spasticity were predominant symptoms. Death occurred on the fourth day. The virus was positive for the equine strain.

CASE 6.—A girl aged 10 years, who lived in Canton, had measles at 2, was vaccinated at 5 and had a tonsillectomy and adenoidectomy in May 1938.

The patient was well until August 22, when she began to complain of persisting pain in the back of the legs. September 4 headache, stiffness of the neck, drowsiness, fever and vomiting developed. Her parents noticed that she talked from the corners of her mouth. She then became stuporous and the next day was admitted to the Norwood Hospital, where a lumbar puncture was done which showed 814 cells, mostly polymorphonuclears, and slightly increased globulin. Prontosil was administered. The patient was transferred to the Haynes Memorial Hospital at noon with a temperature of 104.4 F., pulse rate 120, and respiratory rate 24. She was well developed and well nourished. There was rigidity of the neck and spine and she was lethargic, uncooperative and unresponsive. The skin had a normal appearance. The pupils were equal and reacted to light; the fundi were normal; there was no nystagmus or palsy; the wink reflex was active. The ears were normal. There was no nasal discharge. The pharynx was slightly injected. There were no tonsils. The gag reflex was present. The lungs were normal. The size and position of the heart were normal with a soft systolic murmur, loudest just above the apex. The abdomen was normal. The biceps and triceps reflexes were barely perceptible. The abdominal reflexes were absent. The knee jerks were active, on the right more so than on the left. The Babinski sign was present, bilateral and contralateral on the right leg. The Brudzinski sign was present on the left. The white blood cells numbered 27,550 with neutrophils 80 per cent. Lumbar puncture showed the cerebrospinal fluid to have a pressure of 200, a ground glass appearance, a cell count of 1,205, 61 per cent being polymorphonuclears; protein 83, sugar 72. September 6 the lethargic condition continued; the patient could not be aroused. She was totally relaxed but at times the neck would become rigid. Lumbar puncture was repeated; 14 cc. of cerebrospinal fluid was removed and showed 950 cells. The white blood cell count was 11,350: neutrophils 68 per cent, lymphocytes 28 per cent, endothelial phagocytes 4 per cent. The patient continued to swallow normally. The temperature rose to 108 F., and she died at 4:25 p. m. Treatment had consisted of prontosil and intravenous dextrose.

In this case of encephalitis there were pains in the back of the legs for two weeks before onset of headache, drowsiness, rigidity of the neck and vomiting,

which proceeded to coma and a temperature of 108 F. There were no tremors or muscular twitchings. Death occurred on the sixteenth day of the disease. The virus was positive for the equine strain.

CASE 7.—A boy aged 10 months, living in Randolph, had a negative past history. Whooping cough developed on August 23. Although the paroxysms of typical whooping cough persisted, improvement was noted. He had occasionally lost a meal with the coughing but on the whole had retained his feedings well. The bowels moved normally. September 14 there was no bowel movement and toward evening he became very irritable. Marked sweating and blueness of the arms were noted. There was no muscular twitching or convulsions. He was admitted to the Haynes Memorial Hospital September 15 at 2 p. m. with a temperature of 107.2 F. On examination the baby was well developed and well nourished, was in a stuporous condition and yet responded to stimuli. There was rigidity of the neck. The skin showed a mottled lividity of the limbs and body with general cyanosis. There were staring and vertical nystagmus; the pupils were equal and contracted but reacted to light. The ears, throat and nose were normal. The tongue was dry. Respirations were labored with grunting. There were moist rales throughout the chest but no dullness. The heart was regular, too rapid to count; no murmurs were heard. The abdomen was normal. Knee jerk, abdominal and cremasteric reflexes were absent. The Kernig sign and ankle clonus were absent. No muscular tremors, twitchings or paralyses were noted. The white blood cells numbered 94,500, with neutrophils 27 per cent, lymphocytes 66 per cent, endothelial phagocytes 3 per cent and myelocytes 4 per cent. The red blood cells numbered 6,100,000. Lumbar puncture showed the cerebrospinal fluid to be clear, with a pressure of 108, cells 7, all lymphocytes, globulin was normal, sugar increased. The patient died at 5:25 p. m.

In this case of encephalitis in an infant, occurring at the end of the third week of whooping cough, onset occurred with sudden fever, sweating, irritability followed by lethargy, cyanosis, rigidity of the neck and nystagmus. Tremors, twitching and convulsions were absent. The patient died within twenty-four hours of the onset. Autopsy showed early signs of encephalitis. Results of studies of the virus were negative for the equine strain. Of course, this may be a straight case of pertussis encephalitis, but it occurred within the area of the equine cases, and other infants from this area, proved to have died of this equine virus at other Boston hospitals, have shown similar symptoms and changes in the spinal fluid at the onset, with subsequent changes on the second day similar to those found in our other cases. Consequently, we feel justified in assuming that this patient died before the full picture was established, a phenomenon comparable to the purpura variolosa of smallpox.

CASE 8.—A man aged 50, a shoemaker, on the WPA for two years, who lived in Brockton, had a negative past history. September 12 headache, fever and tremors of the left hand developed. These symptoms improved until September 16. Early on the morning of the 17th a tonic muscle spasm occurred in the right hand and left leg, with complete aphasia. He was taken to the Brockton Hospital and transferred immediately to the Haynes Memorial Hospital. On admission the temperature was 101 F., the pulse rate 104, and the respiratory rate 30. He was well developed and stocky. He was very drowsy but could be aroused. The skin had a normal appearance. There was staring and the eyes rolled outward. The pupils were equal and widely dilated and reacted to light. Corneal reflexes were present. The fundi showed pale disks. The retinas were congested. There were no hemorrhages or tortuosity. The ears were normal. There was no nasal discharge. The jaws were rigid. The fauces was not seen. Respiration was shallow. There were a few coarse rales at the base of the right lung. The size and position of the heart were normal and the sounds

were distant but clear. The blood pressure was 150 systolic, 90 diastolic. The abdomen and genitalia were normal. The extremities showed no edema or lesions. There was marked rigidity of the neck. There was facial palsy on the right side. Flaccid paralysis of the left arm and left leg was present. Tendon reflexes revealed the left biceps greater than the right. Knee jerks were equal and hyperactive. The abdominal and cremasteric reflexes were absent on the left. There was a bilateral Kernig sign and a slight Babinski sign on the left. The right plantar reflex was normal. The Oppenheim, Chaddock and Gordon signs were absent. Ankle clonus was absent. Micturition was involuntary. Urinalysis showed acidity, a large trace of albumin, sugar, a trace of ketone and no bile; the sediment showed an occasional leukocyte and many granular casts. Red blood cells numbered 4,500,000; white blood cells 15,950: neutrophils 89 per cent, lymphocytes 5 per cent and endothelial phagocytes 6 per cent. Chemical analysis of the blood revealed nonprotein nitrogen 50, uric acid 6.1, sugar 154. The Wassermann and Kahn reactions of the blood were negative. The colloidal gold curve was 00012,21000. On lumbar puncture the cerebrospinal fluid gave the appearance of ground glass and had a pressure of 250 and a cell count of 875, with 72 per cent polymorphonuclears. Sugar was normal and globulin was increased.

September 18 the temperature was 104 F., the pulse rate 130, and the respiratory rate 38. On lumbar puncture the pressure of the cerebrospinal fluid was 210 and the cell count was 300: red blood cells 100, white blood cells 200, of which 80 per cent were lymphocytes. The bowels moved naturally. There were a few scattered rales over the back. The clinical diagnoses offered by three members of the staff were (1) cerebral thrombosis with encephalitis, (2) encephalitis with cerebral hemorrhage and (3) cerebral accident.

September 19 the temperature was 100.4 F., the pulse rate 130 and the respiratory rate 30. The patient was more conscious. There was profuse sweating. There were marked tremors of the face, left hand and leg. There was a tremor of the tongue. The pupils were active and equal. The knee jerks were hyperactive and equal. The Babinski, Gordon and Oppenheim signs were absent. The cremasteric reflex was bilateral. The abdominal reflexes were absent. There was marked rigidity of the neck. Aphasia persisted. Fluids could be taken. The blood pressure was 130 systolic, 100 diastolic. White blood cells numbered 17,500: neutrophils 89 per cent, lymphocytes 7 per cent and endothelial phagocytes 4 per cent.

September 20 the temperature was 100 F., pulse rate 120, respiratory rate 30. The patient was even more conscious than the day before. Aphasia persisted. He took fluids well and slept most of the time. Chemical analysis of the blood revealed nonprotein nitrogen 67, urea nitrogen 43, uric acid 6.1, sugar 154. On lumbar puncture the cerebrospinal fluid was clear, with a pressure of 182, a cell count of 100, 94 per cent being lymphocytes and a few red blood cells.

September 21 the temperature was 103 F., pulse rate 140, respiratory rate 60. The patient was in a semicomatose condition. There were numerous moist rales throughout. The clinical diagnosis of the entire staff was eastern strain of equine encephalitis. Daily urinalyses gave the same results as on admission. Chemical analysis of the blood showed nonprotein nitrogen 75, sugar 154. The patient died at 5:40 p. m.

In this case there was gradual onset of encephalitis with remission. Muscle spasm and aphasia developed on the fourth day. There was contralateral flaccid paralysis of the face, arm and leg. Death occurred on the tenth day of the disease. There was a delay of twelve hours in obtaining permission for the autopsy, which may well be the cause of not finding the virus in the brain tissue. In horses it is well known that in order to recover the virus one must place specimens of the brain in 50 per cent neutral glycerin solution immediately after death. Indeed, best results are obtained by veterinarians when the afflicted horse is killed and the brain examined before decomposition sets in.

PATHOLOGY

The brains obtained from patients in this epidemic presented lesions much more acute than any we had previously observed in the several types of encephalitis encountered at the Haynes Memorial Hospital. The disease with which we are dealing is certainly not of the *Economo*, postinfectious or postvaccinal type and can be easily differentiated from them histologically. It corresponds roughly to the picture observed in the St. Louis, Japanese and Winnipeg epidemics, though more severe. The seven cases which came to necropsy consisted of four infants, two children and one adult.

The abdominal and thoracic viscera and associated tissues presented essentially the same gross and microscopic changes, namely a marked general hyperemia, varying degrees of anasarca, slight toxic changes in the liver and kidneys, and a well defined toxic lymphadenopathy and splenitis. The three cases of pertussis showed somewhat divergent pulmonary changes. Case 5 presented the least possible pulmonary edema. A moderate acute bronchitis and early interstitial pneumonitis was present in case 7, while case 4 showed only a mild chronic bronchitis in keeping with the terminal phase of pertussis and an early interstitial pneumonitis. Unfortunately the adult was not examined until twelve hours after death and showed marked post-mortem degeneration. Nevertheless, definite vascular engorgement and moderate senile changes were demonstrable. In view of the marked hyperpyrexia in most of the cases, it is perhaps remarkable that more extensive visceral changes were not encountered.

The macroscopic appearance of the brains was strikingly similar but nonspecific. The vessels of the pia arachnoid were markedly engorged, the finer capillaries standing out as a delicate bright red network. The intensity of vascular engorgement increased from above downward, so that about the brain stem one had to look sharply to be sure there was no actual extravasation of blood. The membranes of the cervical cord showed a definite, though not abrupt, transition from the fiery red of the pons and medulla to a degree of congestion more consistent with the upper surface of the hemispheres. No compression rings were observed. The subarachnoid space usually contained a small amount of slightly turbid, watery fluid in which no frank pus or fibrin could be demonstrated macroscopically. On section the brains were universally softer than normal, this being directly proportional to the degree of histologic involvement. The cut surfaces were varying shades of light to dark salmon pink, against which the engorged vessels stood out prominently. No gross petechiae or thrombi could be demonstrated. The ventricles were consistently normal, containing a small amount of clear fluid and presenting an ependymal surface which was not remarkable. There was no evidence of obstruction to the aqueducts.

Examination of sections from various levels of the central nervous system showed essentially the same microscopic changes. As the congestion and perivascular lesions increased in intensity from the cortex to the brain stem, so the acute disseminate encephalomyelitis reached its maximum intensity of destruction in the basal ganglions, pons and medulla. No part of the brain studied was consistently free from pathologic changes. At present we are unable to correlate the degree of microscopic damage present with the duration of the disease. More comprehensive neuropathologic studies are being undertaken and will be reported later.

At present one may say that cases 1, 3 and 8, each of approximately ten days' duration, presented the most severe lesions, while case 6, of sixteen days' duration, showed only moderate changes. Case 7, of twenty-four hours' duration, presented little more than congestive and edematous phenomena.

The subarachnoid space in all instances contained much serofibrinous coagulum, in the meshes of which were large numbers of lymphocytes, monocytes and neutrophils. The cells varied in proportion at various sites, but in general lymphocytes predominated. The blood vessels which penetrated the parenchyma all showed profound perivascular cuffing with lymphocytes, neutrophils, monocytes and rare plasma cells. Not only were the adventitial lymph spaces stuffed with such cells but they also invaded the surrounding brain tissue to some extent. Many of the Virchow-Robin spaces were filled with extravasated red blood cells, but otherwise only rare petechiae were encountered. The most striking vascular phenomenon in our cases was the frequent predominance of neutrophils in the perivascular accumulations. In addition, many arterial walls were so infiltrated with these cells that the lesion would have to be classified as an acute arteritis. Terminal fibrin thrombi were found in only rare capillaries. No bacteria could be demonstrated in relation to any lesions.

In the more severe cases, all layers of the cortex, basal ganglions, pons, medulla and parts of the cervical cord showed a marked diffuse infiltration with neutrophils, occasional lymphocytes and monocytes and also discrete and confluent areas of profound necrosis infiltrated with similar cells. Degenerations were found in the neurons and neuroglia of each case, but these were not uniform in degree or in distribution. In some instances the pyramidal layer of the cortex presented minute foci of cellular infiltration and glial nodules, but in general the degeneration in the parenchyma did not become extensive until one reached the ganglionic layer. The basal ganglions, pons and medulla presented widely divergent degeneration of the nucleus and tract, scarcely any two of which were similar. In general the median lemniscus, transverse fibers and pontile nuclei suffered heavily, while only occasional lesions of the olivary nucleus were noted. Many of the nuclei of the cranial nerves were involved. Both anterior and posterior horn cells of the cervical cord presented lesions, and the one complete cord examined (case 8) showed slight, but positive, involvement at all levels. Small focal lesions were noted in the molecular layer of the cerebellar hemispheres, but no foci were seen in the nuclear layer. It seems probable that further study may reveal lesions here. Occasional Purkinje cells were destroyed. The cellular degenerations were of virtually every conceivable type, from simple eccentricity and swelling of the nuclei to complete pyknosis, autolysis and neuronophagia. These changes were of course more marked in the cases of greatest severity. No inclusion bodies have been found in any of the sections so far examined.

SUMMARY

Eight fatal human cases of acute encephalitis were observed. All the patients resided in an area where an epidemic of the eastern strain of equine encephalomyelitis involved more than 200 horses during the same period and where mosquitoes were unusually prevalent. Autopsies were performed in seven of these eight human cases, and in four the virus of the eastern strain of equine encephalomyelitis was recovered from the brain.

The clinical diagnosis of encephalitis was made in all cases before death, but by no means was this possible at the onset or until lethargy was pronounced. Hyperpyrexia was a predominant feature. The onset was abrupt in the four infants and more gradual in the older patients, being remittent in two. The clinical course in the older patients was similar to that of the rare severe fulminating forms of human epidemic encephalitis. The clinical laboratory examinations showed wide variations. The blood showed a fairly constant tendency toward a pronounced polymorphonuclear leukocytosis as the disease progressed. The cerebrospinal fluid tended toward a high cell count, but there was no constancy in the predominating cells. Three cases occurred in the course of whooping cough, in two of which the presence of this equine strain of virus was found. The finding of this virus in these two cases confirms the current hypothesis that encephalitis arising in the course of whooping cough can be the result of a superimposed infection.

The virus of the eastern strain of equine encephalomyelitis causes in human beings a profound, acute, disseminate and focal encephalomyelitis characterized by intense vascular engorgement, perivascular and parenchymatous cellular infiltration and extreme degenerative changes in the nerve cells. The gross pathologic manifestations are not specific. In the severe cases the microscopic reaction can readily be distinguished from any of the common types of encephalitis.

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INDUSTRIAL MEDICINE'S CHALLENGE TO THE INTERNIST

RUTHERFORD T. JOHNSTONE, M.D.

LOS ANGELES

Industrial medicine was conceived by the humane forces of an earlier day, which demanded care for the workman with mangled limb, crushed skull or broken back. It was born in the operating room, and its swaddling clothes were bandages and sutures. It was nurtured through the years by the surgeon, with the hygienist and the engineer contributing some of its clothing. Today, in its more mature appearance, it so strikingly resembles its guardian that the profession as a whole recognizes the characteristics of industrial surgery only. The diseases resulting from industrial hazards escaped the attention of the social forces, labor interests and law makers. Occupational disease, usually being insidious in character, lacked the pyrotechnics of trauma.

Inevitably, however, under gradual liberalization, certain states included occupational disease within the compensation code. Today approximately eighteen states admit all, or a specified list, of diseases as compensable if adjudged so. This admission of disease to the code, however, has had little or no effect on the industrial medical set-up, which remains surgical in type. The majority of plants and of railroads and other industries, as well as of insurance carriers, delegate to the surgeon the authority for diagnosis and treatment. Only in rare instances is this responsibility shared with a purely medical confrère. I do not wish to be mis-

understood. I cannot sufficiently praise the industrial surgeon for his development of this branch of service to a high plane. He has no more right, however, to dispose of the occupational disease than has the internist to remove the gallbladder. Nor, in fairness to him, does he desire to do so. Inceptive circumstances forced him into the position he now occupies.

If, as will be illustrated later, the diagnosis of occupational disease requires trained diagnostic ability, why has the internist not been attracted to this field? The roster of industrial surgery is replete with the names of men famous in this field, who stand comparable to the surgeons of general medicine. But where are the Austin Flints, the Peppers, Cabots or Meakins of internal medicine? As indicated in the opening lines, circumstances commandeered the surgeon and he responded nobly, but failure earlier to recognize the extent and the importance of occupational diseases delayed the entrance of the internist. In addition, certain barriers repelled both.

Foremost of these were the stigmas attached to this form of practice. One was made to feel that he was admitting defeat when he entered this field. He was led to believe he had sold his medical birthright for a mess of the charlatan's pottage. Among the unenlightened this opinion still exists. Would that there could be gathered into some vast assemblage the entire profession to hear another Osler panegyricizing the pioneers in this field who shed hypocrisy and criticism, eventually to write one of the most brilliant chapters in modern medicine.

Another barrier has been the pattern of medical education. A few didactic dissertations, crowded grudgingly into a course on preventive medicine and hygiene, constitute the student's sole contact with any phase of industrial medicine. That such contact is negligible is evidenced by the latest report of the Council on Medical Education and Hospitals, in *THE JOURNAL* for April 23, which discloses the fact that, of the seventy-eight medical schools surveyed, only eighteen have a full time department of preventive medicine and hygiene. Only four schools have a course which emphasizes industrial hygiene, and only one that I know of has a course in occupational diseases. Nowhere in that report is the neglect to teach industrial medicine lamented.

It is apparent that the educational system has lacked vision when it is realized that 90 per cent of the students will have industrial contacts at some time in their careers. Postgraduate instruction is similarly missing. At the postgraduate symposium in Chicago last February, every angle of this subject was discussed, but no one championed a graduate course in occupational diseases. Praise was bestowed on the high standard of graduate instruction promulgated by state and county societies, but no one indicated that these groups constantly fail to allot time to occupational disease in their graduate courses. Even conventions held in the name of industrial medicine are not medical but chiefly surgical in character. I have collected twenty programs of meetings held in the name of industrial medicine within the past two years and, of the 198 papers read, only twenty-nine dealt with occupational disease.

The 1936 Fortnightly of the New York Academy of Medicine was a course offered for the study of "trauma, occupational disease and hazards." Of the more than twenty-five papers read, less than five dealt with diseases of occupation. Perusal of the program of the American College of Physicians, which met in April—truly a postgraduate session—fails to disclose a single

From the Special Examination Department, Golden State Hospital. Read before the Section on Preventive and Industrial Medicine and Public Health at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 15, 1938.

correlation between the diseases under discussion and those of occupation. At the California state medical meeting in May, the program of the section on industrial medicine disclosed the ridiculous brevity of six papers. Three were statistical; three were surgical. This is pathetic when occurring in a state where, from the beginning, occupational disease has had a broad coverage in the compensation code.

A third deterrent factor is the indifferent attitude displayed toward this field by the medical press. One suspects that articles on industrial medicine are rejected as so much trivia. If the practitioner is to be informed of existing problems in industrial medicine, it must be through our universally read periodical.

What is this exigency which occupational disease presents? What demand is created by it that the surgeon, hygienist or engineer cannot fulfil? It is diagnosis: diagnosis of innumerable conditions outside surgical experience and beyond the stage of preventive medicine. It is rendered absolutely paramount by the requisites of the compensation law. Basically the same in all states, a condition to be compensable must arise out of and in the course of employment. It must be distinguished from diseases which occur in spite of one's occupation, not because of it. On this distinction rests the whole structure of workmen's compensation. Time prohibits the verbal screening of this pantomime as enacted by occupational disease in the theater of industry. A terse paragraph picturing this parade of paradigms is necessary, however, to further the theme of this thesis.

With the exception of actual trauma, probably the most frequent condition to confront the industrial physician is pain in the lower part of the back. Usually it is not compensable and too frequently is incorrectly diagnosed. Differentiating a sprain of the back from myofascitis, referred pain from kidney or gallbladder, tuberculosis or a malignant condition of the spine, pain in the cord from syphilis or pernicious anemia, a tumor or abscess, or a congenital or structural derangement tests clinical acumen to the fullest. Silicosis may simulate tuberculosis, cardiac decompensation, bilateral bronchiectasis, asthma, a malignant process or mycotic infection. The heart presents prodigious problems in this field. The sudden death of a workman is frequently attributed to trauma, when in reality a fall, injury and subsequent death are often the result of aneurysm, ruptured valves, coronary occlusion or cerebral hemorrhage. Estimation of effort as a causative factor in cardiac accident is a frequent problem in industry, not commonly arising in general practice. The presence of diabetes, syphilis or perivascular disease must be determined in the case of nonhealing fractures, wounds or resistant ulcers. Time prevents discussion of anthrax, actinomycosis, undulant fever and tularemia as occupational conditions. The dermatoses are abundant and confusing. Lead, arsenic and mercury absorption mimic organic disease. The deleterious effects of noxious gases and solvents simulate organic disease.

This brief discussion is only one reel of the entire picture but is sufficient to indicate that the situation demands keen diagnostic perception. Does it seem reasonable that the surgeon, occupied with surgical diseases and trained in surgical technic, should be considered capable? Can the practitioner, neck high in the ills of his community, fill this position? Can the industrial physician, engaged in the practice of some

industrial surgery and some community surgery and in a general practice, be relied on? Is it not obvious that the desideratum is the internist?

A further challenge to the internist from industrial medicine arises out of the present social unrest in America. Social security, old age pensions, unemployment insurance, health insurance and other forms of the vast socialization program will, of necessity, affect industrial medicine. I have stated that only eighteen states today have some form of compensation for occupational diseases. How long is this status likely to prevail? A socially minded government, an ever aggressive labor organization and a socially conscious workman will soon force into being throughout all the states compensation for all types of occupational diseases. When this occurs in the states as yet unacquainted with this problem, what part of the profession can be most quickly relied on to differentiate between communal ills and those arising from industrial hazards? Furthermore, compensation insurance is in grave danger of becoming too broad. Unless the profession has the proper perspective and understands the philosophy behind compensation, this form of practice will extend into social insurance and thence into state medicine. Thus the internist may be the buffer between organized medicine and the actuality of state medicine. On his ability to differentiate the natural ills of life from those arising from occupation may depend the preservation of general practice.

Anticipating the widespread acceptance of the occupational diseases within the compensation code, a few prophetic voices have intimated that when this occurs the burden should be delegated to the community physician. I most emphatically protest that idea. The functions of the general practitioner have been well defined by time and tradition. Seventy-five per cent of the population still depend on him for their care and need him just as he is. To impose on him the additional diagnostic problem entailed by the occupational ills of fifty million workers, not to mention the paper work involved, would overtax his time and capabilities. In addition, in protesting I am mindful of the welfare of the workman and the rights of the carrier. The reason for this objection can be illustrated by a few random cases.

Stooping to pick up a board, a workman experienced disabling pain in the back. cursory examination by his physician resulted in a diagnosis of sprained back; physical therapy was prescribed and ten weeks' compensation awarded. A subsequent check-up revealed a malignant process of the spine.

An employee of a pottery company was sent to a nearby industrial surgeon because of a cough, loss of weight and increasing fatigue. The surgeon's technician made roentgenograms of the chest. The films appeared grossly abnormal. Knowing a silicosis hazard existed where this man was employed, the surgeon combined this fact with the abnormal films and the symptoms to conclude that the man had silicosis. Rest was ordered, and eight months' compensation resulted. Referred examination revealed the pertinent fact that the man was a shipper of the finished, boxed product and had been employed only one year and never before where there was a silicosis hazard. A sister with whom he lived had died two years previously of tuberculosis. Tests of his sputum were positive for tuberculosis, and the roentgenograms showed cavitation but no indication of silicosis.

On the other hand, a woman aged 36, who had been employed for fourteen years by a manufacturer of abrasive soap, consulted her community physician because of severe and increasing dyspnea. Cardiac decompensation was the diagnosis. Complete rest was ordered and digitalis administered. No compensation was awarded. Constant rest and gallons of digitalis resulted in no improvement and a consultation. The girl had advanced silicosis. When informed, her first physician was at a loss to connect soap making with silicosis.

A community physician diagnosed multiple sclerosis as lead poisoning because examination showed lead absorption, which, however, was normal; it did not show any lead intoxication. A baker went uncompensated for ten months for an asthmatic condition due to the wheat flour with which he was in daily contact. I cite these few cases not as indictments against the practitioner but as instances involving factors ordinarily outside his training or experience.

The American Medical Association has wisely insisted that neither the employer nor the insurance carrier shall discriminate against the community physician in favor of one of his own choosing. In full accord, my proposal does not violate that principle. There is no violation of that principle when the family physician refers a patient with an unrecognized heart ailment to the cardiologist for diagnosis. Once the diagnosis is made, the patient returns to his own physician for his after-care. The same policy is carried out with many other conditions requiring a diagnosis. The proposition that I advance is similar. In every city or community let there be formulated a list of the recognized internists or diagnosticians. Have this group certified as to fitness by the American Medical Association. They should be independent of contract or affiliation with any employer or carrier. Permit the employee or patient free choice of any one of this group. A recognized body having thus been established, let every patient with a questionable diagnosis or an estimated temporary disability of two weeks or longer be referred to one of this group for diagnosis. Once that is done, the patient is to return to his community physician for treatment as indicated. If the internist is denied the right to treat the patient, then the existing tendency to make the condition compensable in order to obtain fees for weeks of treatment will be removed. Equity to the workman and the carrier will be assured.

In conclusion, I offer no apology that this paper has not dealt with guinea pigs or test tubes. Medicine needs guidance as well as science. Industrial medicine needs not only guidance but more abundant recognition as one of the important medical specialties. This recognition will not come through the beating of tom-toms by its exponents. It will not come through articles read within this section or appearing only in journals of industrial medicine. It must be obtained by focusing the attention of the entire profession. Nor is the mere expression of thought sufficient. It is time for action by the parent body, the American Medical Association.

The manner of action and the answer to the challenge outlined in this thesis had, I believe, its inception one year ago, when too tardily the Council on Industrial Health was admitted to the American Medical Association. At its first meeting in December it was decided to "proceed slowly." Such a decision is inconsistent with the urgency of the situation. This

council should immediately join with the Council on Medical Education and Hospitals to bring about a readjustment of the medical school curriculum in order that occupational disease may be elevated to proportional importance. It should insist on a fair representation in the postgraduate programs of the county societies as well as in the sectional programs of the state and national meetings. Cooperation with the American insurance group should be sought so that common problems can be solved. Through such mediums—the medical school, the postgraduate system, the medical press and the insurance group—this new body may so function as to induce the present internist, or the future physician, to accept the challenge industrial medicine offers. I confidently anticipate the advent of the occupational disease consultant.

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ABSTRACT OF DISCUSSION

DR. LEOPOLD BRAHDY, New York: We are indebted to Dr. Johnstone for this statement of a deficiency in industrial medicine of which we have all been aware, but no one has previously formulated it or outlined a program to remedy it. The major part of industrial work still is and will continue to be surgical in nature. The medical departments of a few large employers have for many years had consulting internists especially interested in occupational diseases; in other words, the occupational disease consultant has arrived, although until now he has had no specific name and still lacks recognition. What Dr. Johnstone advocates is coming to pass, though much too slowly. In Mexico I found that occupational diseases have long been accepted as a definite medical specialty, and the medical school of Mexico University devotes more time to this subject than any of our schools. In 1935, at the International Congress on Occupational Disease and Injuries in Belgium, two things that bear on this question impressed me: first, the small proportion of Americans (I think the total number was six); secondly, that our colleagues of other lands who specialized in occupational diseases held important positions in their profession, their medical schools and their governments, much more than those in this specialty in the United States. This confirms Dr. Johnstone's thesis of the need of better recognition in the United States. The presence of consultants in occupational diseases of the medical staff of a few large employers is not sufficient. About half of all production is by small employers, those who have 200 employees or less. Such employers necessarily seek medical advice from the community physician, the same physician who takes care of their workers' injuries. These practitioners, even if they attended one of the few medical schools that have courses in industrial hygiene, cannot be experts on cases they so seldom see. These physicians should consult specialists in occupational disease problems, just as they consult brain surgeons or ophthalmologists. When an occupational disease consultant is to be found in every industrial community and adequately recognized, these smaller plants which employ the majority of our workers will be able to obtain the benefit of expert advice. Specialization in occupational disease by the internist is essential because the field is large and expanding. Diagnostic ability is the keystone of the specialty. The physician must not only diagnose any known occupational disease; he must be able to recognize promptly a new clinical entity, one just born as a by-product of the dizzy multiplication of industrial products and methods. To do that necessitates a degree of clinical acumen which cannot be required of the busy practitioner. A course in occupational diseases should be part of every medical curriculum.

DR. DWIGHT O'HARA, Boston: I wish to say a word in defense of the medical school curriculum. This call for more time is not unique; it has come within recent years from a dozen groups who have settled down to the job of expanding their own interests. I do not imply that such expansion is not salutary, but the recommendation that medical school courses be expanded to include more didactic instruction in these special

lines is against the present trend in medical education. The call is now for less rather than more didactic instruction. We do not believe that we can make any kind of specialists by haranguing our classes for sixteen, thirty-two or sixty-four hours in special subjects. We already cover much of industrial medicine in other courses. A Colles fracture is the same whether it is sustained in the kitchen or in the factory and lead poisoning is the same, wherever the lead arises. Other courses emphasize channels of entry and the influence of age and sex for most industrial poisons. I favor the development of industrial medicine but in the same way that I do the development of preventive medicine; that is, as a point of view in a much larger conception of environmental influence. Also there is a point of diminishing returns in the development of any specialty. When any specialist who does not deal directly with the chest becomes so specialized that he allows himself to make the statement that he "knows nothing about chests," he ceases to be as effective a doctor as he was before he forgot what little he may have learned about chests in the medical school.

DR. AUGUST F. KNOEFEL, Terre Haute, Ind.: Having been born and raised with the industrial commission in our state, I enjoyed the remarks that have been made. The previous discussor said that there is no difference between the Colles fracture of the man at the plant and the one of the wife at home. There is a big difference, and that is the psychoneuroses that attended the fracture at the plant. It makes a big difference when the time for adjudication comes up. There is a place for this organization. My reaction is that if it is to do the greatest good it should become more scientific and less sociologic. There are doctors who still believe that if a person chews a lead pencil he will have lead poisoning. That may be an exaggeration. A person walks through a public garage and the next day has a headache, nausea and vomiting—carbon monoxide poisoning. All a man has to do to testify before an industrial commission is to be a graduate of medicine and registered in his state. We can bring in the thyroid expert or some one who knows things from A to Z, but his testimony is of no more value legally than the testimony of the individual who lives out in Podunk.

DR. A. T. McCORMACK, Louisville, Ky.: We are hearing about the necessity of devoting more time in the undergraduate courses to training for the specialties. I attended the other day a conference on maternal health in Washington and was impressed with the fact that the speakers, several of whom had each had thirty years' experience as teachers of obstetrics in great state universities, testified that there was practically no one in their states qualified to deliver a woman, that only those who had passed an examination by the American Academy of Obstetrics were so qualified, and formal resolutions were passed that nobody could be called in consultation in obstetric cases unless he had that qualification. I am sympathetic with the idea that the man who holds himself out as a specialist should know his subject. The fact, however, has been brought out that 75 per cent of all the ills that mankind has had have been treated by the general practitioner; and yet among the medical schools of the United States there is only one, so far as I know, that has a general practitioner in the faculty, and that is the Albany Medical College. I believe that if we teach the student while in school in his premedical, cultural education, while he is in the technical school, enough facts on which he can base the ability to observe and to reason from his observations, we have done as much for him as we can. Let's put the emphasis on graduate work for the men peculiarly adapted to the specialties which we want our disciples to be taught and to learn. There can be no question that the internist is important, that he has a distinct and definite place in the vast field of industrial medicine. But only that internist will really succeed who, in addition to his scientific knowledge, has the ability to differentiate the different psychoses, the different neuroses, the selfishness and sordidness of the people who come before him, and to exclude those things that need to be excluded and to keep before him this whole complex situation which has been brought about by our compensation laws and other things. Let's not get the idea that we are going to be able to develop, full fledged from our undergraduate medical schools, specialists who will make any serious contribution to human welfare.

CHILLING OF THE BODY SURFACES

ITS RELATIONSHIP TO AURAL AND SINUS INFECTIONS

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It is doubtful whether any subject in medicine in the last decade has stirred more interest and caused more study than the etiology of infections of the upper part of the respiratory tract. Through recent improved understanding of the autonomic nervous system, the biochemical processes and the bacterial flora constantly present in the nasal cavity and its adnexa, much of the fog of empiricism has been dispelled. A cardinal factor not to be ignored, however, is that the human organism must maintain a constant average temperature of 98.6 F. (37 C.), for any considerable degree of deviation from this average for appreciable periods of time will result in morbid changes.

Cold water has a veritable appetite for heat. Since the ratio of conductivity of water to air is 27 to 1, it follows that water takes heat from the body twenty-seven times faster than does air. The lack of a compensating mechanism for the maintenance of an average normal temperature in any medium colder than his normal surroundings is conspicuous in man. Many arctic birds maintain a normal temperature above 102 F. (38.9 C.) throughout continued periods of exposure to icy waters, as do also the arctic Mammalia, yet man's loss of body heat during submersion for only fifteen or twenty minutes in water at a temperature of 70 F. (21.1 C.) may be five times the normal basal rate. Mudd, Goldman and Grant¹ reported the striking effect of this loss of body heat on the nasal mucous membranes. In their experiments, carried out by placing in the nares a sensitive instrument devised for registering temperature, they recorded depressions as great as 10.8 degrees F. (6 degrees C.), their observations indicating the great amount of vasoconstrictor response in this area.

This tendency to rapid loss of heat owing to physical conditions that promote such loss forms the basis for this study. Its practical application relates to the ordinary causes of the common cold, in particular bodily immersion such as swimming and bathing, and also exposure to excessive cooling by drafts, from damp clothing and the like.

One of us² observed the effect of chilling on 250 children under 13 years of age by taking their temperatures before and after a period of forty-five minutes' duration devoted to swimming in an indoor pool with the temperature of the water at 73 F. (22.8 C.). In only thirty of this number was a normal temperature maintained; in many there occurred a drop to as low as 95 F. (35 C.).

It has been brought out previously that well tended swimming pools do not constitute the bacterial menace often attributed to them. Bacteria are of course normally and constantly present in the upper respiratory

Read before the Section on Laryngology, Otology and Rhinology at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 16, 1938.

1. Mudd, S.; Goldman, A., and Grant, S. B.: Reactions of the Nasal Cavity and Postnasal Space to Chilling of the Body Surface, *J. Exper. Med.* 24: 11 (July) 1921.

2. Taylor, H. M.: Sinusitis and Swimming, *J. A. M. A.* 85: 7 (July 4) 1925.

passages, but they may multiply to pathologic proportion in the person whose resistance is lowered.

Kuntz³ made clear the interrelation of the innervation of the peripheral blood vessels and the mucous membranes. This autonomic control of vasoconstriction and vasodilatation forms the basis of the physiologic balance between the splanchnic and the peripheral areas. Thus, when stimulation by cooling results in peripheral ischemia, the mucous membranes undergo a similar experience; prolongation of this condition serves to throw out of balance the nicety of integration existing under normal metabolic phases and accounts for the ability of ordinarily avirulent organisms to overcome the obstacles of tissue immunity at the portals of entry.

EXPERIMENTAL STUDIES

In the present study the most important single factor regarding the establishment of infection is that during exposure peripheral vasoconstriction is prevented by

the three animals a second exposure to cold caused an even more decided leukopenia than at first.

Moon, Lieber and Kennedy⁵ noted that, when histamine-like substances are present in the blood, a leukocytosis occurs. This observation would seem to indicate that in the cases observed by us, in which leukopenia developed in both animals and human beings after chilling in the absence of muscular activity, there was no histamine allergy to cold such as that recently reported by Horton and Roth.⁶

In connection with his work as a member of the Committee on the Otorhinologic Hygiene of Swimming of this section of the American Medical Association, one of us⁷ reported in 1936 the observations on a group of swimmers that are set forth in table 2. Eight lifeguards at Jacksonville Beach, Fla., were subjected to swimming for forty-five minutes in ocean water at a temperature of 68.5 F. (20.3 C.). The weight, temperature, blood pressure and blood count of each swim-

TABLE 1.—Changes in the Hemogram of Guinea Pigs After Chilling

	Animal 1			Animal 2			Animal 3		
	Before	After*		Before	After		Before	After	
		1st Test	2d Test		1st Test	2d Test		1st Test	2d Test
.....	8,230	6,850	6,750	9,850	7,400	7,250	8,900	6,500	4,400
.....	78	40	67	82	77	49	68	39	44
.....	19	60	32	18	23	51	30	57	53
.....	3	1	1	..
.....	1	5	3	3
.....	1

* Time elapsing between exposure tests about one-half hour.

TABLE 2.—Effect on Blood Cell Count in Marathon Life Savers' Race, Jacksonville Beach, Fla., Sept. 9, 1935

Name	Before							After						
	Red Blood Cells	White Blood Cells	Juveniles	Stab Cells	Segmented Cells	Lymphocytes	Monocytes	Red Blood Cells	White Blood Cells	Juveniles	Stab Cells	Segmented Cells	Lymphocytes	Monocytes
DeLoach.....	4,530,000	7,450	0	25	44	31	0	5,130,000	18,200	18	73	73	1	0
Perkins.....	4,520,000	5,700	0	23	34	34	1	5,340,000	19,900	23	63	63	0	0
Horton.....	4,448,000	6,700	0	26	52	20	0	3,820,000	21,750	26	67	67	0	0
Penn.....	4,580,000	11,000	0	26	48	26	0	5,360,000	33,750	30	53	53	15	0
Miller.....	4,610,000	8,500	0	30	40	30	0	5,420,000	17,200	35	44	44	12	0
Crenshaw.....	4,210,000	5,050	0	31	41	28	0	4,650,000	30,400	7	35	51	6	0
Clark.....	4,680,000	6,700	0	20	45	33	0	5,350,000	18,900	50	34	12	0	0
Liddell.....	4,480,000	8,600	0	6	58	35	1	5,580,000	12,250	12	66	20	0	0

muscular activity, and it follows that infection is therefore less likely to occur. In an experiment with animals, three healthy, mature guinea pigs, weighing approximately 250 Gm. each, were placed for half-hour periods in an ice refrigerator in which the temperature was 59 F. (15 C.). As soon as they were removed, blood counts were made with specimens of freely flowing blood from the veins of the ear. The observations made and previously recorded are set forth in table 1 to show the rather striking changes occurring in the hemogram.

The conclusions to be drawn from this experiment are that chilling without exercise produces a leukopenia of the polymorphonuclear neutrophilic type. As stated by Trommsdorff,⁴ the phagocytic powers of the blood cells are definitely diminished. This observation was further substantiated by the death of one of our animals within twenty-four hours, and at autopsy the presence of bronchopneumonia was noted. In each of

mer were ascertained prior to and immediately after the period of swimming. All the participants after the swim exhibited a diffuse generalized purplish hue. Their nail beds were moderately cyanotic, as were their lips. There was an average reduction of 4 degrees F. in the rectal temperature. The increase in the erythrocyte count ranged from 700,000 to 1,500,000 red cells. The leukocyte count was consistently increased by from 3,650 to 24,750 white cells. The Schilling index was virtually normal. There was no loss of weight. Both the systolic and the diastolic blood pressures were increased, but the greater average rise was in the diastolic pressure, being from 20 to 30 points. There was no such consistent increase in the systolic pressure.

In a third experiment, made at Jacksonville, Fla., in September 1937, three bathers remained submerged in a pool for fifty minutes, keeping reasonably quiet

5. Moon, V. H.; Lieber, M. M., and Kennedy, P. J.: Histamine and Leukocytosis. *Arch. Path.* 20: 175 (Aug.) 1935.

6. Horton, B. T., and Roth, Grace M.: Collapse After Swimming. *Proc. Staff Meet., Mayo Clin.* 12: 7 (Jan. 6) 1937.

7. Taylor, H. M.: Report of Committee on Otorhinologic Hygiene of Swimming. *Tr. Sect. Laryng., Otol. & Rhin., A. M. A.*, 1936, p. 300.

3. Kuntz, Albert: The Autonomic Nervous System in Relation to Otolaryngology. *J. A. M. A.* 107: 334 (Aug. 1) 1936.

4. Trommsdorff: *Arch. f. Hyg.* 59: 1, 1906.

by refraining from exercise. The temperature of the water was 72 F. (22.2 C.). The observations set forth in table 3 indicate the distinctly depressive effect of chilling the body surfaces without concomitant exercise. The polymorphonuclear leukocytosis, so evident in the second experiment, was totally lacking here; indeed there was even a relative leukopenia, both as to the total number of white cells and as to the polymorphonuclear neutrophil count. It was also observed that the temperature of the body tended to drop and the pulse rate to slow.

CONCLUSION

It is evident from these experiments that chilling of the body surfaces without compensation leads to morbid changes within the body. They are caused (1) by peripheral vasoconstriction with attendant peripheral stasis and anoxemia, (2) by lowered leukocyte response, both total and polymorphonuclear, and (3) by impairment of the phagocytic capabilities of the fixed tissue cells, including that of the nasal mucous membrane.

TABLE 3.—Effects of Chilling Without Concomitant Exercise

Name	Temperature*		Pulse Rate		Blood Pressure		Total Leuko-cyte Count	
	Before	After	Before	After	Before	After	Before	After
Pittman	98.3	95.4	80	63	120/80	125/90	8,500	8,400
Fortson	98.3	97.0	70	72	118/80	120/88	9,250	8,150
Horton	98.3	97.0	70	60	120/80	130/80	7,100	6,300

* Temperatures were taken by rectum.

One of the immediate results of these changes is the predisposition to infections of the upper part of the respiratory tract, the paranasal sinuses, the eustachian tubes and the middle ear.

111 West Adams Street.

ABSTRACT OF DISCUSSION

DR. EDWARD CECIL SEWALL, San Francisco: The authors have shown the physical changes caused by the chilling of the body. He has suggested that the blanching of the respiratory surfaces makes one liable to respiratory disease. I am in general agreement but believe that the discussion may be amplified and qualified. One must distinguish between normal persons and those who harbor chronic sinus infection. I believe that, ordinarily, chilling only induces respiratory disease in those who already harbor respiratory infection, most often in the sinuses. The normal person is but little adversely influenced by a reasonable degree of chilling. Such a person is exemplified by John Muir, who, soaked to the skin, slept on Alaska glaciers repeatedly. He arose in the morning, wrung out his clothes and went his way. He rarely took cold. He was a normal, healthy person. He harbored no chronic sinus infection. He could not have exposed himself in such a way if he had. He carried an immunity granted by his last true "cold" from which he had fully and completely recovered. He was vulnerable to upper respiratory infection only when that immunity had run its course, ordinarily varying from six months to several years. With lapse of his acquired immunity, chilling might have favored susceptibility to respiratory infection. Even that, however, is open to question, as common experience shows that true colds travel with little reference to chilling and exposure. I constantly find and study people of this type who are free from all sinus infection. Usually sturdy folk, they are little influenced or inconvenienced by chilling. The great majority of people, however, harbor chronic sinus infection. It is in this type that the work of the authors is of great importance. Such individuals have been shown by Kistner and others to harbor bacteria constantly in the deeper layers of their sinus mucosa. These germs are held in leash by the forces of immunity generated in the body and carried in the blood. They always act as irritants. Under warm climatic and other favorable influences the bacteria show little

activity, measured by the amount and character of the discharge they always produce. Chilling of the body, as Drs. Taylor and Dyrenforth have shown, causes certain physical changes that relax the vigilance of the body guards toward these incorrigibles. The latent bacteria show immediate activity. Some of you already may have recognized the effect of our local summer "refrigerating system" of fog and brisk sea breeze.

DR. JOHN J. SHEA, Memphis, Tenn.: To comprehend this paper it is necessary to study it in detail after reading the papers that have been written relative to the hygiene of swimming. There exists in the human body a mechanism that controls heat production and elimination, a second system that is a barrier controlling the migration of blood cells from the hematopoietic system into the general circulation, and third a biochemical balance that maintains our normal pH irrespective of whether we take foods that are acid or foods that are alkaline. Whenever one of these is disturbed all three of them will be disturbed and in the chilling action the heat mechanism is influenced, which in turn disturbs this barrier, of the physiologic action of which little is known. There is always stored up in our hematopoietic system sufficient matured and immatured blood cells so that if they accidentally migrate into the peripheral circulation there will be a blood dyscrasia. The answer to why we are susceptible to colds after chilling may be this interrelationship between the hematopoietic system and the buffer, which maintains our biochemical balance. The application of the paper is this: If any one of us would wrap ourselves in a wet blanket and go into the basement of our home for forty-five minutes or an hour we would certainly end up with a cold or possibly pneumonia, provided we harbored the proper bacteria. A child subject to recurrent infections of the sinuses, middle ears and mastoid should avoid the promiscuous habit practiced at these pools of children playing in wet bathing suits, which lowers their resistance and brings about a recurrence of sinusitis or middle ear infection. The child who goes to California or Florida in the winter to convalesce from these infections should not be allowed to swim or even wade but should limit his activity to the beach.

DR. BURT R. SHURLY, Detroit: Since the days of the vulnerable heel of Achilles, we have known that many individuals have a peculiar idiosyncrasy to a chilling of the body. This chilling is commonly caused by a draft on the feet, when low shoes are worn, or when the feet have inadequate protection. There is the chilling after a haircut and shampoo, the chilling from insufficient clothing, the susceptibility to chilling after the sun goes down, with the attendant development of the common cold or congestion of the turbinates, with various hyperemic manifestations of change. We know that sensitivity to cold is not as common as sensitivity to heat. The former can be relieved by the application of heat or by exercise. Persons with heat sensitivity react during the warming up process but are made worse by heat. In 1909 Wallace reported a case in which, after the ingestion of ice cream and a glass of cold water, a severe attack of asthma, watery discharge from the nose and eyes, cyanosis, urticaria and collapse occurred. Probably diathermy or some other form of heat, mental exercise or excitement would have relieved the paroxysm. Asthma caused by cold, as well as urticaria, is related in many case reports. It is not uncommon to find a nasal mucous membrane sensitive to local heat relieved in a refrigerated room, by a cold compress or by the inhalation of cold air. In some persons thermic sensitivity is closely related to infection, rising with slight changes in the weather. The true infection may be simulated by these sharp reactions. This is not always lowered resistance but a lack of vasomotor tone in the thermoregulators of the body. Some of it is endocrine in its lack of response; some of it is in those who carry a chronic infection of the sinuses or manifest allergic phenomena. These persons become forewarned by experience; they have chilling after prolonged bathing or swimming, with a cyanosis and skin reactions, a lowered temperature, from 92 to 95 F., which denote a failure in vasomotor response to chilling of the body. The old treatment—a mustard foot bath with 10 grains of quinine and 10 grains of Dover's powder—was an ancient therapeutic measure to counteract the common cold. The reinforcement of circulatory deficiencies has for years

been recognized by the use of the hot lemonade or a hot toddy at bedtime following chilling of the body. The first stage of pneumonia—a congestion of the lung—should be met with prompt therapeutic action or even a hypodermic sedative to restore the vasomotor action.

DR. H. MARSHALL TAYLOR, Jacksonville, Fla.: Dr. Sewall comments on the fact that Mr. Muir was peculiarly free from sinus infection during his arctic adventures. As long as one can maintain his normal temperature in such an environment, his resistance is not necessarily lowered.

EDUCATION A MAJOR NEED IN ADEQUATE MEDICAL CARE

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Adequate care for the sick presupposes the existence and the use of adequate facilities. Both economics and education are integral parts of the problem of adequate medical care. If the economic structure of society were such that all could afford adequate service, many would not get it through lack of proper information. The individual must be able to recognize the need of seeking service, he must avail himself of the resources available, and either he or some one for him must finance the service. Care by physicians, dentists, hospitals and nurses and the providing of pharmaceutical products are the chief needs, and the bulk of all moneys expended are for these services.

Disease is of two types, the acute and the chronic. The demands made by chronic illness are greater because of the long periods of disability and often because of the patient's failure ever to resume his customary work. If the patient is the supporter of a family, the situation is even worse.

In the older communities, in which, because of the age distribution, many of the citizens are incapacitated with chronic disease, the problem is becoming a real burden on the community. If the community is to attempt a control of chronic disease, it must avail itself of all information at its disposal regarding the problem. Data from the Massachusetts survey of chronic diseases and the Massachusetts cancer program are presented in this paper in the hope of partially clearing up some of the confusion on the subject.

The eradication of chronic diseases is extremely improbable, but to secure delay in the onset of some of these diseases and to prevent others seems a reasonable objective. Studies have shown that the onset of many of these diseases occurs to too great an extent in early middle life. In the Massachusetts study of chronic diseases approximately 20 per cent of persons between the ages of 40 and 50 were found to be affected. If the age of onset could be extended to beyond 60, the twenty year increase in the span of health would mean increased working efficiency, lower bills for sickness, less drain on the family income and improved general well being of the individual.

In considering the needs of the American people for medical attention, the mere chronicling of the diseases present, such as has been done in the majority of surveys, gives a reasonably reliable measure of morbidity and the percentage of the population which does not receive medical treatment. Of those who do not receive medical care, however, there are some who do not need it, such as the blind man and the one-legged

man. In planning any program for improving the condition of persons not receiving medical care, this factor needs consideration.

Another factor of importance is the adequacy of the service of persons who are receiving medical attention. Do they receive as much care from the physician as is necessary? How well is the physician able to meet their demands? Other phases of the problem require a discussion of hospitalization, nursing care, dental care, cost of pharmaceutical products and the cults.

The scope of this paper is limited to the presence or absence of medical care during a one year period among persons with chronic disease. The number of physicians' calls is not considered, nor is the adequacy of the therapy administered.

In the survey of chronic diseases conducted by the Massachusetts Department of Public Health in 1930, records were obtained from 15,000 persons over the age of 40. Of this number 4,337 (28.9 per cent) admitted having one or more chronic diseases. Of the sick, 63.7 per cent were under the care of physicians, 2.3 per cent were cared for by the various cults and 33.9 per cent had either self-administered treatment or no treatment. Subdivided according to economic status, those with a comfortable income employed physicians in 80.5 per cent of the cases, those with a high moderate income in 69.7 per cent, those with a low moderate income in 63.2 per cent and the poor in 58.6 per cent.

TABLE 1.—Reasons for Lack of Medical Care Among Persons
Who Had Received No Care for One Year

Reason	Comfortable	High Moderate	Low Moderate	Poor	Total
Felt condition not serious.....	6	46	159	23	234
Felt physician could not help.....	3	54	289	92	438
Fear.....	0	1	4	2	7
No faith in physicians.....	0	4	30	21	55
Economic reasons.....	0	0	43	56	99
Other reasons.....	1	2	18	4	25
Unknown.....	0	8	8	4	20
Total.....	10	115	551	202	878

All the diseases and disabilities were not necessarily of equal importance in respect to the need for medical care. An attempt was made to separate the persons having conditions which it was felt required a physician's care from those for whom a physician could do little or nothing. This separation was necessarily arbitrary, but for practical purposes the group remaining after the persons with conditions which were not normal but for which there was probably little or no need of medical care were withdrawn is a far better criterion of the need for medical service. This group comprised 3,266 persons (21.8 per cent of the surveyed population). When subdivided by an economic basis, 20.1 per cent of those with a comfortable income were sick and 82 per cent of the sick had employed physicians during the preceding year, 19.8 per cent of those with a high moderate income were sick and 74.6 per cent of the sick had employed physicians, 20.9 per cent of those with a low moderate income were sick and 70.8 per cent of the sick had employed physicians, while 28 per cent of the poor were sick and 65.4 per cent of the sick had employed physicians. If treatment at the time of the survey had been used rather than medical care during the past year, the rates would be much lower but also less descriptive. The persons who had had no care during the preceding year were questioned as to their reasons (table 1).

If the figures for the reasons "felt condition not serious," "felt physician could not help," "fear" and "no faith in physicians" measure the need for education, approximately 80 per cent of the persons who did not employ a physician during the past year required education. If the reasons for delay are applied to the sick who needed physicians (3,266), the rates indicate that economic factors are not as important as education.

TABLE 2.—Reasons for Not Having Physicians, Percentages

Reason	Comfortable	High Moderate	Low Moderate	Poor	Total
Need of education.....	13.5	19.4	23.7	22.1	22.4
Economic reasons.....	0.0	0.0	2.1	9.0	3.0
Others and unknown.....	1.5	1.8	1.3	1.3	1.4
Had irregular practitioners...	3.0	4.2	2.0	2.2	2.4
Had physician.....	82.0	74.6	70.9	63.4	70.7
Total.....	100.0	100.0	100.0	100.0	99.9

TABLE 3.—Reasons for Delay

Reason	Percentage of Those Who Delayed	Percentage of Total
Negligence.....	76.2	42.1
Fear.....	5.8	3.2
Economic reasons.....	4.5	2.5
Miscellaneous.....	13.5	7.5
Less than two months' delay.....	44.7
Total.....	100.0	100.0

The need for a better informed public at all economic levels is indicated. Among the poor, approximately 10 per cent were deterred from having medical advice during the preceding year by financial reasons. Again it must be emphasized that having medical care does not measure adequate medical care. The interesting observation is that among the poor who had not employed physicians, those who gave reasons which indicated a need for education were twice as many as those who furnished economic reasons.

As confirmatory evidence, the ten year experience in the Massachusetts cancer clinics is cited. Massachusetts has conducted free diagnostic clinics for cancer for over ten years; free hospitalization has been furnished for the indigent and low cost hospitalization (\$10.50 a week) for those able to pay. Free pathologic service has been given, and an educational campaign, based on the thesis that the local physician shall be the instructor to his community, has been in operation since 1934. There is no reason why any person should not receive an adequate diagnosis of cancer and adequate therapy provided he knows the need for seeking service and is willing to avail himself of the facilities.

The experience in Massachusetts demonstrates most conclusively that the keynote of cancer control is education. Records have been obtained from 4,159 persons who came to the diagnostic clinics and have since died of cancer. The living patients were not tabulated, but it is believed, on the basis of other studies, that if they had been included the results would not be far different. Of the 4,159 patients, 44.7 per cent delayed less than two months in consulting a physician after noting the first symptoms. Two months may be considered too long an interval to classify as no delay, but it has been arbitrarily chosen. Negligence was given as the reason for delay by 42.1 per cent of the patients, fear was given by 3.2 per cent, economic reasons by 2.5 per cent and miscellaneous reasons by 7.5 per cent. The only explanation for the percentage who furnished economic reasons would appear to be prudishness about using the state clinics, inability to

find transportation to the clinics or lack of knowledge of their existence. The last-named reason bespeaks a need of more education.

After going to the clinic and receiving a diagnosis, some patients delayed further, although 85 per cent received treatment within one month.

Of the 227 persons who never reported for treatment, over one fourth were unwilling to admit the diagnosis of cancer. An additional 4 per cent claimed negligence, while 8 per cent complained of fear. If these rates are combined in the estimate of the need for further education, even for those who attended the clinics, 37.4 per cent of those who never accepted treatment were impelled by this reason, contrasted with 1.5 per cent who furnished economic reasons. These methods of appraisal indicate that a large part of the need for medical care is due to lack of demand, primarily because of failure to recognize and utilize the available service.

As a measure of what can be accomplished by intensive education, the experience of the Massachusetts cancer clinics is again cited. The intensive program began late in 1934, and a comparison of the years from 1934 to 1937 in the state as a whole and in organized communities is made. In towns where the cooperative cancer control committees are functioning well, there has been an increase of 44.6 per cent in patients with cancer referred by physicians, while in the state as a whole, including both organized and unorganized communities, the increase is 22.4 per cent. The percentage of persons who went to their physicians within the first two months of illness increased between 1934 and 1937 in the organized communities by 31.8 per cent, while in the state as a whole it increased by 27.3 per cent. The number of persons who came to the cancer clinics during the first five months of their disease increased 15.9 per cent in the organized communities

TABLE 4.—Period of Delay Between Diagnosis and Treatment (Massachusetts State-Aided Cancer Clinics)

Reported for treatment within:	Percentage
1 week.....	57.5
2-4 weeks.....	27.5
2 months.....	4.8
3 months.....	1.8
4 months and over.....	2.9
Did not report.....	5.5
Total.....	100.0

TABLE 5.—Reasons for Persons Dying of Cancer Without Reporting for Treatment (Massachusetts State-Aided Cancer Clinics)

Reason	Percentage
Unwillingness to admit diagnosis.....	25.1
Negligence.....	4.0
Fear.....	8.0
.....	1.5
.....	38.3
.....	3.5
Miscellaneous.....	18.5
Total.....	100.0

and 3.2 per cent in the state as a whole. The number of physicians who use the pathologic service has tripled in the organized communities, while in unorganized communities it has only slightly more than doubled. This observation is especially significant because in some of the organized communities new pathologic services have been started.

It would seem that the method used in Massachusetts in combating cancer might well be extended to include other chronic diseases. The physicians of the com-

munities attempt to educate the people, and the state, in turn, furnishes supplementary service for the patients of the physicians.

SUMMARY

1. Of 3,266 persons with chronic disease whose records indicated the need for medical attention, 878 did not have a physician during one year preceding the survey.

2. For every one who gave his economic status as a reason for not employing a physician, 7.47 gave reasons which pointed toward a need for more information. Among the poor, this ratio was reduced to 1 giving economic reasons to 2.46 needing education.

3. Over half the persons who attended the Massachusetts cancer clinics delayed over two months, and the majority of them gave reasons which pointed toward a need for more education. The Massachusetts program cares for the economic needs, but the problem of delay is still acute.

4. The experience of the Massachusetts cancer clinics with persons who delayed obtaining treatment after diagnosis showed a similar need.

5. As a result of an intensive educational campaign on cancer conducted in Massachusetts for the past three and one-half years, part of the need for medical service has been reduced. A further reduction seems extremely probable.

CONCLUSIONS

The type of program conducted in combating cancer might be extended to other diseases. Whether the Massachusetts cancer program will be successful in other states remains to be seen (several are now trying it). Whether an extension to other diseases elsewhere is practical is problematic.

Clinical Notes, Suggestions and New Instruments

SEVERE HYPERCHROMIC MACROCYTIC ANEMIA OF PREGNANCY

CHARLES G. BARNUM, M.D., AND JOSEPH C. WOODWARD, M.D.
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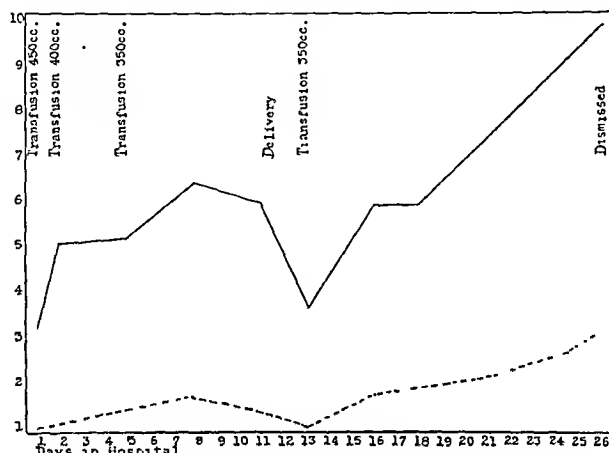
Mrs. A. R., an Italian housewife, aged 34, admitted to the hospital May 22, 1936, was a sextipara and septigravida, with parturition due May 30. For the previous two months she had noticed increasing weakness. Two weeks before admission she had begun to experience almost constant nausea, with frequent vomiting, and since then she had remained in bed. The weakness had increased to the point of dyspnea and palpitation on moving in bed. The skin had become yellowish and the urine scanty and dark. The bowels moved infrequently; the stools were brown, and there had been no diarrhea. For the previous week she had noticed numbness and tingling over the anterior surface of the right thigh, and on the day before admission she had a sudden attack of numbness involving the right side of the face and the right arm.

The diet had been low in protein and vitamins for economic reasons.

The patient's first child died shortly after birth. Since then she had had five normal pregnancies and no miscarriages. She had an appendectomy and oophorectomy in 1926. In 1930 she had suffered from rheumatism but had had no symptoms since. There was no history of syphilis, rat bite or exposure to industrial poisons. She had not received medication recently by mouth or by injection. The family history was entirely irrelevant.

At examination the temperature was 98 F., the pulse rate 96, the respiratory rate 20 and the blood pressure 135 systolic,

65 diastolic. The patient, who was obese, was sitting propped up in bed and was dyspneic on slight exertion. The skin was dry, with a lemon yellow tinge. There were no purpuric spots or petechiae. The hair was gray and scanty. The fundi showed retinal pallor; the mucous membranes of the mouth were pale; the teeth were in fair condition, and the tonsils were atrophic. The thyroid was normal, and there was no adenopathy. The breasts were pendulous, the lungs clear and the heart not enlarged. The sounds were distant but of fair quality. A soft systolic murmur at the apex was not trans-



The solid line shows the hemoglobin content (grams per hundred cubic centimeters, Sahli) and the broken line the red blood cell count (millions per cubic millimeter).

mitted. The pulmonic second sound was normal, and the aortic second sound was not heard. The pulse was soft and regular, with a rate of 96. The abdomen was obese. The fundus was 6 cm. below the xiphoid process. The fetal heart rate was 130, heard in the left lower quadrant. The head was not engaged. The liver, spleen and kidneys were not palpable. There were no masses and no evidence of ascites. The extremities were normal. Neurologic examination gave negative results.

A catheterized specimen of urine was amber, cloudy and acid, with a specific gravity of 1.016. Examination showed a trace of albumin, no sugar, acetone, diacetic acid or bile and a normal amount of urobilin. Microscopic examination showed an occasional granular cast and an occasional white blood cell and epithelial cell. Study of the blood showed hemoglobin content 3.5 Gm. (Sahli), red cells 1,300,000, color index 1 and white cells 5,000, with 80 per cent polymorphonuclears, 18 per cent lymphocytes and 2 per cent monocytes. The red cells stained deeply. Anisocytosis, macrocytosis, and polychromatophilia were observed. The polymorphonuclear neutrophils showed a shift to the right. The platelets appeared reduced. No parasites were seen. The Wassermann and Kahn reactions of the blood were negative. The nonprotein nitrogen content of the blood was 30 mg. per hundred cubic centimeters. The icteric index was 13. In the bromsulphalein test for hepatic function no dye was retained (negative reaction). The delayed direct Van den Bergh reaction was very faintly positive, and the indirect reaction was very faintly positive. The stool was brown and gave a negative reaction for occult blood, ova and parasites. An analysis of the gastric contents during fasting showed a free hydrochloric acid content of 10 degrees and a total acid content of 23 degrees. After the patient had taken 50 cc. of 7 per cent alcohol, analysis showed a free hydrochloric acid content of 40 degrees and a total acid content of 53 degrees. Tests were negative for blood, lactic acid and micro-organisms.

The patient was given three transfusions of citrated blood, totaling 1,200 cc., and received 3 cc. of liver extract intramuscularly every other day. Symptomatically she was much improved but her blood picture did not respond well, as shown in the accompanying chart. On the tenth day in the hospital vitamin B therapy in the form of two brewers' yeast tablets three times a day was started. On her eleventh day the membranes ruptured spontaneously, and after three hours of labor

she was delivered of a normal male infant weighing 6½ pounds (2,948 Gm.). She lost very little blood during delivery and there was no shock. Oxygen and ether were administered intermittently during labor and the delivery. On the second postpartum day the patient appeared tired and pale. Her pulse rate was 110 and the quality was rather poor at times. The blood picture showed a return to the level of admission. She was given another transfusion of 350 cc. of citrated blood and the following day appeared much improved. Liver extract was given every other day, and she received six brewers' yeast tablets daily. She made a rapid recovery and was discharged from the hospital on June 18.

The infant weighed 7 pounds 12 ounces (3,515 Gm.) on discharge. A blood count done on its fourth day showed the hemoglobin content 22.2 Gm. (Sahli), red cells 6,000,000, white cells 5,000 and differential count normal. On smear the red cells were seen to be uniformly large and deeply stained.

One year later the patient's blood picture was checked by Dr. E. R. Comstock and was found to be normal. She had had no complaints during the interval. No liver or vitamin therapy was used during this time.

COMMENT

A search of the literature, including the work of authors from India,¹ New Zealand,² France,³ South America,⁴ Italy⁵ and the United States⁶ reveals some agreement on the treatment of this condition but marked differences of opinion on its cause. The incidence varies from one for 10,000 pregnancies in the temperate zones to twenty-nine for 1,000 pregnancies in India. The clinical picture is that of acute anemia developing during the third trimester of pregnancy. Pallor and extreme weakness are constant symptoms. A low grade fever occurs in 80 per cent of the cases. Vomiting and diarrhea are common; the latter is said to indicate a poor prognosis. Dyspnea and edema occur late. Paresthesias are often noted, but no definite lesions of the cord have been found. There may be glossitis, splenomegaly, hepatomegaly and occasionally purpura. A lemon-yellow color of the skin is uncommon. Laboratory examination shows severe hyperchromic anemia, the hemoglobin content usually being below 6 Gm. per hundred cubic centimeters, with a high color index. The blood chemistry is essentially normal. The stools show nothing of significance, although they may be watery and sometimes foamy. The urine usually contains a trace of albumin, rarely more than 0.5 per cent; casts in moderate numbers are observed. Urobilin is not present. Gastric acidity may be normal, reduced or absent. As to cause, no specific disease has been constantly associated with this condition. Many different theories have been advanced, but few have any concrete evidence for substantiation. Castle and Strauss⁶ expressed the opinion that the

mechanism of production is similar to that of true pernicious anemia. Wills¹ has shown that massive doses of liver extract will produce a reticulocyte response comparable to that of pernicious anemia, but she also found that vitamin B in the form of a yeast extract (marmite) was equally effective in producing regeneration of the blood.

Blood transfusion is the most important single item of treatment, as patients with this condition are desperately ill and may die of myocardial failure before a satisfactory response to liver or vitamin B therapy can be obtained. The mortality rate for untreated patients runs as high as 90 per cent; while with adequate treatment a mortality rate as low as 10 per cent can be obtained. Termination of pregnancy is generally agreed to be contraindicated. Efforts should be directed toward improving the patient's condition before she goes into labor. Iron, arsenic and vitamins A, C and D have been shown to be without value.

Fetal death in utero is common, but if the fetus lives until term the prognosis is good. The infant's blood picture is normal.

Special Clinical Article

THE DIAGNOSIS AND TREATMENT OF
WOUNDS OF THE HEART

A REVIEW OF TWENTY-TWO CASES

CLINICAL LECTURE AT SAN FRANCISCO
SESSION

DANIEL C. ELKIN, M.D.

ATLANTA, GA.

Wounds of the heart demand early diagnosis and operation, for delay is rapidly fatal. Every attempt at accurate diagnosis should be made before operation, since exposure of the heart is in itself hazardous. The occasion for cardiorrhaphy arises rarely and always in cases in which immediate intervention is required; therefore the surgeon should have in mind the definite principles involved in the diagnosis and treatment. The object of this paper is to review twenty-two cases in which operation was performed and to set out certain principles based on that experience.

GENERAL CONSIDERATIONS

Incidence.—Wounds of the heart are relatively rare. At the Medical College of Virginia Hospitals 0.1 per cent of surgical patients had such injuries,¹ and in my own experience² approximately 2 per cent of penetrating wounds of the chest injured the heart. Considering the size of the heart in relation to the chest and its exposed position, it is surprising that it is not more frequently injured. If patients who die of cardiac wounds but never reach the hospital were considered, the percentage would probably be much higher.

Weapons Producing Wounds.—All the patients in this series were Negroes. Wounds were produced either with a knife (fifteen cases) or an ice pick (seven cases). The type of knife is one generally referred to as a "switch blade," with a thin 4 inch blade. No patients with gunshot wounds of the heart have been treated, for the reason that they usually die from hemorrhage before reaching the hospital.

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Read in the Surgical Division of the General Scientific Meetings at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 14, 1938.

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14. Castle, W. B., and Strauss, J. H.: Pernicious Anemia of Pregnancy, J. Clin. Invest. 1: 297-300 (June) 1931.

Location of Wounds.—The approximate location of the wounds is shown in the accompanying diagram. As is to be expected from the position of the heart in relation to the anterior wall of the chest, wounds of the right ventricle are more numerous; but wounds of all four chambers, as well as of the intrapericardial portion of the aorta (two cases) and pulmonary artery (one case), have been encountered. The location of the wound is of no importance so far as symptoms are concerned, and the exact position can only be surmised before operation, but it is of prognostic importance for reasons which will be mentioned later.

DIAGNOSIS

History.—Symptoms are due to tamponade and loss of blood. The former is of great importance because of the narrow margin of safety under which the heart works. A rapid change in the pressure relationships of the heart affects its filling and emptying and thereby leads to cerebral anemia and death. All the patients in this series had tamponade of the heart, and in a majority of instances there was a history or evidence of external bleeding or blood was found in large quantities in the pleural cavity. Death may occur from hemorrhage without the establishment of tamponade, but I have not seen it do so.

The history is usually characteristic. Bleeding is profuse at first, with no other symptoms for several minutes. During this period the patient suffers no effects of the injury. One of my patients "ran three blocks," another "walked several hundred feet" and a third was able to "fight for about ten minutes." This phase is followed by exhaustion and collapse, frequently with unconsciousness. Occasionally a raving delirium (thought due to cerebral anemia) develops. At the same time there is usually a cessation of bleeding from the external wound. This chain of symptoms is due to gradually developing tamponade. When the heart is wounded it bleeds freely to the outside or into the pleural cavity. At the same time blood collects in the pericardial cavity. When from 100 to 200 cc. has collected the pericardium becomes distended, the intrapericardial pressure rises and the venae cavae can no longer empty normal quantities of blood into the heart. The heart, being unable to fill to capacity, can no longer empty, and cerebral anemia results.

Physical Appearances.—The patient has usually been comatose or in a state of wild delirium when brought to the hospital. The position and direction of the external wound are of some importance in diagnosis, but the course of a knife thrust is notoriously misleading, although those just to the left of the sternum from the second to the fifth interspaces are most apt to injure the heart. Careful probing of the external wound may show by pulsation of the instrument that the heart is injured.

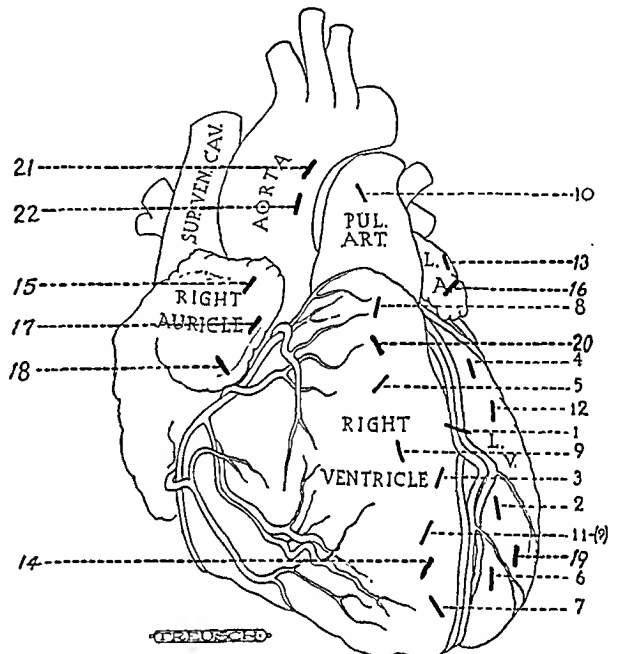
The skin is cold and moist. Because of the venous congestion, there is marked pallid cyanosis of the lips and tongue. The heart sounds are muffled and distant, and the pulse weak or absent.

Arterial and Venous Pressure.—The arterial pressure is lowered or unobtainable and the venous pressure is raised, as evidenced by the struffed prominent external jugular veins. The estimation of the venous pressure is of value in determining the extent of the tamponade and the progress of cardiac compression. A normal venous pressure is generally considered to range between 75 and 125 mm. of water. A pressure as high

as 340 mm. has been seen and is consistent with life if not maintained for too long a period. The venous pressure rapidly drops with release of the tamponade, and the arterial pressure rises.³ Readings of the venous pressure are of value after operation in cases in which the reaccumulation of blood or fluid is suspected in the pericardium. They should be made with the needle and manometer on a level with the heart and with the patient in a horizontal position.

Roentgenographic Examination.—Roentgenograms of the heart are of no value, since death may occur from an amount of blood too small to cause a noticeable change in the size and contour of the cardiac shadow.

Fluoroscopic examination, as pointed out by Bigger,¹ is of great value, since an accumulation of blood in the pericardial sac prevents normal pulsations. Of all the



The approximate point of cardiac injury in the twenty-two cases reported.

diagnostic methods this is the most accurate both in proving and in disproving one's suspicions of cardiac tamponade. It had best be done at the bedside with a portable fluoroscope, since moving the patient may increase the bleeding.

Electrocardiograms.—These are of little value in establishing a diagnosis, since normal tracings may be obtained for several hours after an injury, but are of aid in determining the extent and progress of infarction after suture of the wound.⁴

Summary.—A lowered or falling arterial pressure, a high or rising venous pressure and the absence of cardiac pulsations by fluoroscopic examination make the diagnosis of tamponade practically certain. In the cases here presented the diagnosis was made before operation in each instance. No patient was needlessly subjected to operation.

OPERATION

After a diagnosis is established, immediate operation should be carried out. Danger of infection and the frequent deaths from this cause demand the most

3. Elkin, Daniel C.: Wounds of the Heart, *J. Thoracic Surg.* 5: 599 (Aug.) 1936.
4. Elkin, D. C., and Phillips, Heywood: Stab. Wound of the Heart; Electrocardiographic Studies of Two Cases, *J. Thoracic Surg.* 1: 113 (Dec.) 1931.

meticulous care in the preparation and the carrying out of the operation under a rigid aseptic technic. However, no time should be wasted, and for this reason the operating room should be set up as soon as the presence of a cardiac wound is suspected. In order to save time, all the instruments needed for an operation on the heart are kept in a separate container and sterilized by autoclave. While preparations are made for operation, the patient should be kept as quiet as possible by administration of morphine. External heat should be applied and the patient's head lowered. Infusion of saline solution, transfusion and measures which tend to raise the blood pressure are of little or no value if tamponade is present and may do harm in increasing the hemorrhage. The administration intravenously of a 6 per cent solution of acacia should be given when the operation is begun. Autotransfusion of citrated blood is of value as an emergency measure and may be done during the operation. Blood transfusion should always be performed as soon as possible after operation.

auricles or great vessels, the incision may be continued across the sternum and the pectoral muscles on both sides, retracted, and a portion of the sternum removed, if necessary for a proper approach to the wound. An excellent and inexpensive instrument for cutting the sternum is the ordinary blacksmith's horseshoe clipper. A third method, and one giving excellent exposure, consists of turning a flap of skin and muscle laterally and removing two or more costal cartilages.

With any type of incision, the internal mammary vessels are ligated and divided, the triangularis sterni muscle is divided, and the lung and pleura are displaced outward by gauze dissection. If time permits, every effort should be made to avoid injuring the pleura, since the collapse of the lung adds greatly to the shock. The wound in the pericardium is then located and enlarged, or, if the wound is not readily found, the pericardium is opened between stay sutures. If tamponade exists, the pericardial wound is usually bleeding slightly, if at all, but when the intrapericardial pressure is released, bleeding becomes marked and the

TABLE 1.—Summary of Twenty-Two Cases of Cardiac Wounds.

Case No.	Sex	Age	Instrument	Period from Admission to Duration to	Location	Result	Cause of Death	Survival Period	Comment
1	♂	18	Knife	30 minutes	R. ventricle	Recovery	Well 7 years
2	♂	25	Knife	40 minutes	L. ventricle	Recovery	Well 8 years
3	♂	41	Knife	30 minutes	R. ventricle	Death	Pericarditis	3 days	Necropsy; wound healed
4	♂	25	Knife	"Few min."	L. ventricle	Death	Hemorrhage	None	Large wound; died on table
5	♂	30	Knife	?	R. ventricle	Recovery	Well 4 years
6	♂	30	Knife	"Few min."	L. ventricle	Death	Pneumonia	2 days	Necropsy; wound healed
7	♂	21	Knife	30 minutes	R. ventricle	Recovery	Well 3 years
8	♂	32	Knife	Not known	R. ventricle	Death	Emphysema	14 days	Mediastinal emphysema
9	♂	27	Knife	60 minutes	R. ventricle	Recovery	Well 3 years
10	♂	24	Ice pick	Not known	Pul. artery	Death	Pneumonia	2 days	Necropsy not done
11	♂	34	Knife	Not known	R. ventricle?	Recovery	Well 5 years
12	♂	22	Ice pick	Not known	L. ventricle	Death	Bacteremia	36 hours	Necropsy; wound healed
13	♂	36	Ice pick	"Few min."	L. auricle	Recovery	Well 2 years
14	♂	30	Ice pick	"Few min."	R. ventricle	Recovery	Well 2 years
15	♂	20	Knife	15 minutes	R. auricle	Recovery	Well 15 months
16	♂	43	Knife	Not known	L. auricle	Death	Hemorrhage	None	Died from hemorrhage at operation
17	♂	36	Knife	30 minutes	R. auricle	Death	Infection	3 days	Necropsy not done
18	♂	22	Knife	1 hour?	R. auricle	Death	Hemorrhage	None	Died from hemorrhage at operation
19	♂	30	Ice pick	Not known	L. ventricle	Death	Pneumonia	2 days	Necropsy; wound healed; pneumonia
20	♂	30	Knife	Not known	R. ventricle	Recovery	Well 11 months
21	♂	28	Ice pick	"Few min."	Aorta	Recovery	Well 2 months
22	♂	..	Ice pick	Not known	Aorta	Death	Pneumonia	2 days	Necropsy not done

Inhalation anesthesia is preferable for several reasons. The pleura may be accidentally opened during the operation or already opened by the wound, and nitrous oxide and oxygen under positive pressure is necessary for the inflation of the lung. When the tamponade of the heart is released there is usually a recovery of consciousness, and the patient will become excited, struggle and interfere with the procedure at the most inopportune time.

The incision should be planned to secure the best exposure in the quickest time and with the least shock. Some idea as to the position of the wound in the heart may be obtained from the position of the external wound, but the course of a stab wound is notoriously misleading. The medium sternotomy (Duval-Barasty) gives excellent exposure of the heart and the great vessels and by this approach the pleura is less likely to be opened. However, it requires a great deal of time, as does the closure of the wound, and is productive of shock. In the event of severe hemorrhage or increasing tamponade, the patient would not be likely to survive such a procedure.

The intercostochondral thoracotomy (Spangaro) offers a rapid approach to the heart but not a particularly good exposure. It can be enlarged by cutting or removing the cartilages above and below the incision and by removing a portion of the sternum. In wounds near the base of the heart or in those involving the

contractions of the heart increase in force. With the release of the tamponade the arterial pressure rises and the venous pressure drops. The greatest difficulty in suturing the wound is in the placing of the first stitch. This is facilitated by removing the blood by suction and, when the wound is located, by placing the index finger of the left hand over it. By this method the flow of blood will be impeded sufficiently to allow the passage of a suture directly beneath the finger. This is left untied and is held in the left hand for traction and hemostasis. The wound can then be readily sutured and closed completely. Fine black silk on small full curved needles is the material of choice. The sutures should pass into the substance of the muscle but not into the chambers of the heart. This procedure is difficult in the thin-walled aorta and pulmonary artery or in the auricles, but suture material inside them is apt to be the starting point of a clot which may prove fatal. Wounds located in the edges of the heart, on its posterior surface or behind the sternum are best reached by placing an apex suture as advocated by Beck.⁵ By this method the heart may be rotated and the wound brought into position. After control of the hemorrhage, the pericardium is cleansed of clots by flushing with physiologic solution of sodium chloride. The peri-

5. Beck, Claude S.: Wounds of the Heart, Arch. Surg. 13: 205 (Aug.) 1926.

cardium is closed with interrupted sutures of silk, space being allowed for the drainage of fluid, which is sure to accumulate. The muscle, fascia and skin are closed carefully in layers without drainage.

PROGNOSIS

The immediate prognosis depends largely on the interval between injury and operation. Delay may cause death from hemorrhage or tamponade or both. It likewise depends on the character and extent of the injury; a bullet usually causes two wounds, with greater hemorrhage and loss of tissue. The postoperative prognosis is dependent on infection, purulent pericarditis and pneumonia, as will be seen from the summary of cases (table 1). All except three patients survived the operation but died from complications in periods ranging from one to fourteen days (table 2).

Of the twenty-two patients, eleven died and eleven recovered. This mortality of 50 per cent is approximately the average for the cases reported in the literature up to this time. The percentage of recoveries is questionable because of the fact that many single cases with a favorable outcome have been reported, whereas those ending fatally are not so apt to be recorded.

The location of the wound is of prognostic importance. As will be seen from table 3, there were eight wounds of the right ventricle and six of the patients recovered. On the other hand, of the six patients with wounds of the left ventricle only two recovered. This is probably due to the fact that the operative approach to the right ventricle and the suture of this chamber are easier. Wounds of the auricles and of the intra-

TABLE 2.—Cause of Death

	Number Died
Hemorrhage.....	3
Pericarditis, infection.....	3
Pneumonia.....	4
Emphysema.....	1
Total.....	11

TABLE 3.—Location of Wound

	Total Patients	Recovered
Aorta (Intrapericardial).....	2	1
Pulmonary artery (intrapericardial).....	2	0
Right auricle.....	3	1
Left auricle.....	2	1
Left ventricle.....	6	6
Right ventricle.....	6	2
Total.....	22	11

pericardial portion of the aorta and pulmonary artery are more hazardous because of the difficulty of approach and because of the difficulties of suturing these thin-walled structures.

SUMMARY

The diagnosis of a wound of the heart can be made with practical certainty from the history, the arterial and venous pressure and the fluoroscopic examination.

The operative treatment should be carried out immediately.

The prognosis is dependent on the interval elapsing between the time of injury and the institution of treatment and on the postoperative complications, mainly infections. Wounds of the right ventricle offer a better prognosis.

50 Armstrong Street.

Special Article

HUMAN REQUIREMENTS OF VITAMIN C

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WASHINGTON, D. C.

The following is the thirty-first and the concluding article in the present series on vitamins, published under the auspices of the Council on Foods and the Council on Pharmacy and Chemistry. This series of articles will be published in book form.—Ed.

It was early found that about twice as much vitamin C is required to prevent the first appearance of microscopic alterations in the teeth as to prevent the outward symptoms of scurvy in guinea pigs. It was also observed that in infants and children receiving enough vitamin C for protection against scurvy there may still develop a condition of latent or subacute scurvy accompanied by more or less severe injury to the teeth. It then became apparent that considerably larger quantities of vitamin C are required for good nutrition than for the prevention of scurvy.¹

The first attempt at using human beings as subjects for the determination of requirements of vitamin C was made in Sweden in 1931 by Göthlin,² who measured the capillary resistance or fragility of two forcibly fed schizophrenic subjects during a period on a liquid diet which at first was devoid of vitamin C and later supplemented with increasing quantities of orange juice until the lowered capillary resistance was barely restored to normal. This point was reached on daily intakes of 0.7 and 1 cc. per kilogram of body weight respectively. Translated into modern terms, this would correspond to from 21 to 30 mg. of ascorbic acid for an adult weighing 60 Kg., or about 132 pounds. In Göthlin's opinion the disturbance in the strength of the capillaries as measured by his blood pressure method corresponds to the microscopic alterations in the teeth of guinea pigs as measured by the Höjer³ tooth structure method, and by relating these two methods he concluded that a man weighing 60 Kg. requires from fourteen to twenty times as much vitamin C as a guinea pig weighing 300 Gm. for corresponding protection. When ascorbic acid became available Göthlin⁴ used it in place of orange juice in this indirect method of determining human requirements with resulting values of from 19 to 27 mg. daily—quantities surprisingly close to the value of from 21 to 30 mg. calculated from the direct experiments on human subjects.

This indirect method, however, has received less attention since knowledge of the chemical identity of ascorbic acid has made possible more or less satisfactory tests for its identification, and its availability in quantity has led to its use in metabolic studies with determinations in the urine and blood subsequent to the ingestion or injection of known quantities of the vitamin. Following the now classic studies of Harris and his asso-

1. Sherman, H. C., and Smith, Sybil L.: The Vitamins, ed. 2, New York, Chemical Catalog Company, 1931, chap. IV.

2. Göthlin, G. F.: A Method of Establishing the Vitamin C Standard and Requirement of Physically Healthy Individuals by Testing the Strength of Their Capillaries, *Skandinav. Arch. f. Physiol.* **61**: 225 (May) 1931.

3. Höjer, J. A.: Method for Determining the Antiscorbutic Value of a Foodstuff by Means of Histological Examination of the Teeth of Young Guinea Pigs, *Brit. J. Exper. Path.* **7**: 356 (Dec.) 1926.

4. Göthlin, G. F.: Human Daily Requirements of Dietary Ascorbic Acid, *Nature* **131**: 569 (Oct. 13) 1934.

ciates,⁵ Johnson and Zilva⁶ and Hess and Benjamin⁷ on the relation of urinary excretion to the intake of vitamin C as determined by indophenol titration, and of King and his associates,⁸ Gabbe⁹ and Farmer and Abt¹⁰ on the significance of the concentration of ascorbic acid in blood as determined by the same indicator with certain modifications in technic, the outlook seemed encouraging toward the close of 1934 for the establishment of definite standards for judging vitamin C nutrition and requirements for various age groups. As is often the case, however, the problem has become more rather than less complicated with increased study. This is due chiefly to the fact that thus far no entirely specific method has been developed for the chemical determination of ascorbic acid. Among the numerous reports that have been published during the past three years there have been quite as many dealing with difficulties in methodology as with definite requirements. Brief mention of the more important sources of error in the determination of ascorbic acid in blood and urine has been given in a previous paper of the series.¹¹ Space does not permit the detailed discussion of methodology, which is almost necessary for the evaluation of data on which present recommendations of requirements are based. The problem is still further complicated by the multiplicity of methods that have been used to interpret data on metabolism in terms of quantitative requirements as reviewed in the following section.

METHODS OF DETERMINING THE REQUIREMENTS OF VITAMIN C

The state of vitamin C nutrition in human beings is determined by one or more of three measurements: (1) the resistance or fragility of the blood capillaries, (2) the excretion of ascorbic acid in the urine and (3) the content of ascorbic acid in the fasting blood. To make use of these measurements for the estimation of requirements of vitamin C involves the acceptance of certain standards based on repeated observations on healthy normal persons.

Capillary Resistance or Fragility.—In this method the strength of the blood capillary system is measured on the upper arm by the positive pressure technic of Göthlin¹² or by the negative pressure technic of Dalldorf.¹³ It was at first anticipated that this would prove to be a very practical method for survey work in estimating the vitamin C nutrition of large groups of people, but this has not proved to be the case, in this country at least. The literature on the use of the method has been reviewed recently in THE JOURNAL.¹⁴ Since then, papers dealing with the usefulness and limitations of the method have appeared from the laboratories of both Göthlin and Dalldorf.

According to Göthlin,¹⁵ the capillary fragility test serves as a measure of the physiologically indispensable minimum requirement of vitamin C, for it can be used to determine the quantity of the vitamin necessary to maintain the capillary system on the borderline between a normal and a weakened condition. The test is also useful in detecting a rather severe degree of vitamin C undernutrition. From simultaneous tests for capillary fragility and the determination of the ascorbic acid content of the fasting blood it has been shown that at this borderline of capillary strength the ascorbic acid content of the blood lies between 0.1 and 0.14 mg. per hundred cubic centimeters, values considerably below the generally accepted minimum normal value of about 0.6 mg. per hundred cubic centimeters. Consequently there is a degree of vitamin C deficiency within the range in ascorbic acid content of the blood of from 0.1 to 0.6 mg. which cannot be detected by the capillary fragility test. In Göthlin's opinion the reason the capillary fragility test is considered of little value as a means of detecting vitamin C undernutrition in certain countries, while in Sweden where his work has been done it has been found so satisfactory, is that in countries where there is an abundance of vitamin C-containing foods blood values seldom fall as low as 0.14 mg. per hundred cubic centimeters, and consequently there is no reaction with the capillary fragility test. In Sweden, however, during the long winter months the vitamin C content of the diet is so low that capillary fragility develops in thousands and the test is very useful as a means of detecting the most severe deficiencies.

A more clinical slant to the problem is given by Sloan from Dalldorf's hospital laboratory.¹⁶ Applying the test with negative pressure technic to several normal subjects, two subjects with bleeding but no scorbutic symptoms and a fairly large group of patients with all degrees of scorbutic symptoms from simple bleeding of the gums to severe scurvy, he has concluded that the capillary resistance test in the majority of cases gives dependable information concerning the presence or absence of vitamin C depletion but does not indicate the degree of depletion and gives falsely negative results in the presence of severe anemia.

Urinary Excretion of Ascorbic Acid.—The twenty-four hour output of ascorbic acid in the urine as determined by indophenol titration according to various modifications of the original Tillmans method¹⁷ has been used more generally than any other value as a measure of vitamin C nutrition and excretion after test doses as a means of calculating requirements. In the early work of Harris and his associates¹⁸ the term "resting level" of vitamin C was used to indicate the day-by-day excretion of the vitamin, with a value of about 10 mg. representing the borderline between deficiency and adequacy, 20 mg. a moderately low intake and 40 mg. a liberal intake of the vitamin. Somewhat later, on finding that adult subjects on a daily intake of 25 mg. of ascorbic acid, selected as representing the "minimum-optimal" requirement, excreted about 13 mg.

5. Harris, L. J.; Ray, S. N., and Ward, A.: The Excretion of Vitamin C in Human Urine and Its Dependence on the Dietary Intake, *Biochem. J.* 27: 2011, 1933.

6. Johnson, S. W., and Zilva, S. S.: The Urinary Excretion of Ascorbic and Dehydroascorbic Acids in Man, *Biochem. J.* 28: 1393, 1934.

7. Hess, A. F., and Benjamin, Helen R.: Urinary Excretion of Vitamin C, *Proc. Soc. Exper. Biol. & Med.* 31: 856 (April) 1934.

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14. Dalldorf, Gilbert, and Russell, H.: The Effect of Cytotoxic Acid Injections on Capillary Resistance, *Hollis: J. A. M. A.* 104: 1701 (May 11) 1935.

15. Göthlin, G. F.: The Present Status of Vitamin Deficiencies in Practice, *J. A. M. A.* 108: 15 (Jan. 2) 1937.

16. Sloan, R. A.: A Comparison of Methods for Detecting and Grading Subclinical Scurvy, *J. Lab. & Clin. Med.* 23: 1015 (July) 1938.

17. Tillmans, J.; Hirsch, P., and Hirsch, W.: Das Reduktionsvermögen pflanzlicher Lebensmittel und seine Beziehung zum Vitamin C, *I. Der reduzierende Stoff des Citronensaftes*, *Ztschr. f. Unters. d. Lebensmitt.* 63: 1 (Jan.) 1932.

18. Harris, L. J.; Ray, S. N., and Marrack, J. R.: Tissues and Its Determination, *J. Biol. Chem.* 103: 687 (Dec.) 1933.

19. Harris, L. J.; Ray, S. N., and Marrack, J. R.: Diagnosis of Vitamin C Subnutrition by Urine Analysis: Quantitative Data, *Lancet* 2: 1399 (Dec. 21) 1935.

daily, the Harris group¹⁹ concluded that if a subject excretes less than 13 mg. of ascorbic acid a day and fails to respond by a marked increase in excretion on the first or second day to a test dose of 700 mg. per 10 stone (140 pounds, 63.5 Kg.) of body weight, his diet has contained less than the reputed minimum-optimal quantity of vitamin C. This excretion value of 13 mg. a day is often used without further qualification as a standard of adequacy, but, since it represents an intake within the range of the physiologic minimum requirement established by Göthlin,² as noted earlier, it should be considered as indicating the borderline of adequacy rather than an optimum condition. According to van Eekelen,²⁰ a daily excretion of 40 mg. indicates that the subject is in a state of vitamin C saturation.

It has been recognized from the first that a better picture of vitamin C nutrition can be obtained by the so-called test dose or saturation method than by a determination of the resting level of excretion alone. Briefly, this method consists in determining the daily excretion during a period in which large doses of ascorbic acid are given to saturate the tissues. In the use of the method there has been little agreement as to general procedure and interpretation. Opinions differ as to the size of the test dose, the method of administration, the end point of saturation and the final calculation of the data.

A dosage of 700 mg. per 10 stone (140 pounds) of body weight, as first recommended by Harris and his associates,¹⁹ has been used most frequently, although doses as low as 100 mg. and as high as 1,000 mg. have been reported. When the ascorbic acid is taken by mouth, as is commonly the case, the excretion of 50 per cent or more of the entire test dose within twenty-four hours, or of the half-day dose within twelve hours,²¹ is commonly used as the criterion of saturation, although this will depend on the size of the test dose, for the larger the dose the lower the percentage excreted. This makes it difficult to compare observations of different investigators who have used test doses varying in size.

It has been shown that the peak of excretion of ascorbic acid in the urine occurs within from four to six hours following oral administration,²² and within from one to three hours following intravenous administration.²³ Subcutaneous injection is preferred to intravenous by van Eekelen and Heinemann,²² who consider that when the test dose is given intravenously the concentration in the blood is raised so suddenly that a transitory overflow into the urine results before the tissues are saturated. In their experience a test dose not exceeding 300 mg. when given subcutaneously to a saturated subject, is entirely excreted within six hours, with the peak occurring just before the end of

the third hour. According to Baumann,²⁴ the best insight into the behavior of saturation is obtained by the oral administration over several days of small doses of ascorbic acid (50 mg. for small children, and 100 mg. for older children and adults). Under such conditions healthy persons excrete from 60 to 80 per cent of the test dose on the third or fourth day. He has noted a wide range in the saturation capacity of different persons as thus determined—the span ranging from 0 to 40 mg. of ascorbic acid per kilogram of body weight.

A difference has been shown recently in the behavior of various persons to continued administration of ascorbic acid after the saturation point has been reached, as shown by a sudden and marked increase in excretion of ascorbic acid. Instead of additional increases with continued high doses, as might be expected if a real state of saturation had been reached, Hamel²⁵ found in some instances no further rise for several days. This plateau of excretion, indicating a disappearance of ascorbic acid after the body reservoirs had been filled, he attributed to a form of specific dynamic action, which should be taken into consideration in estimating requirements by the test dose method.

As a qualitative survey method for determining the state of vitamin C nutrition of large groups of subjects, the test dose method in its simplest form is undoubtedly of some value, as will be shown later. Advantage has been taken of the time interval before the peak of excretion has been reached after oral administration of the test dose to shorten the period of collection of urine in routine surveys of school children.²⁶ In the application of the method to the determination of the extent of vitamin C undernutrition of any age group, various procedures have been followed. The total quantity of ascorbic acid required before saturation is reached is sometimes referred to as the "saturation deficit," and the extent of this deficit is considered an index of the nutritional status of the subject with respect to vitamin C.²⁷ The number of days required to reach saturation on a given test dose serves as another index.²¹ If a prolonged period on a vitamin C free diet precedes the saturation tests, the difference between intake and excretion up to the point of saturation is considered to be a measure of the maximum tissue reserves of the subject.²⁸

Of the various procedures that have been developed for the application of the test dose method to the determination of actual requirements of vitamin C, two or three will be described in some detail as representative of methods designed to determine vitamin C requirements ranging from minimum to maximum or representing barely adequate to presumably optimal nutrition. At the lower end of the scale may be considered a method developed by Widenbauer²⁹ and used in an extensive investigation of human requirements. In a preliminary period of several days, during which the subject is kept on a uniform diet containing very little vitamin C, the titration value of the urine is determined

24. Baumann, T.: Die Bestimmung der physiologischen Spanne der C-Vitamin Sättigung des Organismus, *Klin. Wchnschr.* **16**: 1246 (Sept. 4) 1937.

25. Hamel, P.: Ueber die Vitamin C-Bilanz des Menschen: II. Belastungsversuche zur Bestimmung des täglichen Verbrauches und des Sättigungsdefizits, *Klin. Wchnschr.* **16**: 1105 (Aug. 7) 1937.

26. Harris, L. J., and Abbasy, M. A.: Nutrition Surveys: A Simplified Procedure for the Vitamin-C Urine Test, *Lancet* **2**: 1429 (Dec. 18) 1937.

27. Gauder, J., and Niederberger, W.: Ueber den Vitamin C-Bedarf alter Leute, München, med. Wchnschr. **83**: 1387 (Aug. 21) 1936.

28. O'Hara, Patricia H., and Hauck, Hazel M.: Storage of Vitamin C by Normal Adults Following a Period of Low Intake, *J. Nutrition* **12**: 413 (Oct. 10) 1936.

29. Widenbauer, F.: Der Vitamin C Haushalt des Menschen unter verschiedenen Verhältnissen, *Klin. Wchnschr.* **16**: 609 (April 24) 1937.

19. Harris, L. J.; Abbasy, M. A., and Yudkin, J.: Vitamins in Human Nutrition: Vitamin-C Reserves of Subjects of the Voluntary Hospital Class, *Lancet* **1**: 1488 (June 27) 1936.

20. van Eekelen, Marie; Emmerie, Adrianus, and Wolff, L. K.: Ueber die Diagnostik der Hypovitaminosen A und C durch die Bestimmung dieser Vitamine im Blut, *Ztschr. f. Vitaminforsch.* **6**: 150 (April) 1937.

21. Jezler, A., and Kapp, H.: Zur Frage des Vitamin C-Defizits, *Ztschr. f. klin. Med.* **130**: 178 (June 10) 1936.

22. Hawley, Estelle E., and Stephens, D. J.: Rate of Urinary Excretion of Test Doses of Ascorbic Acid, *Proc. Soc. Exper. Biol. & Med.* **34**: 854 (June) 1936. van Eekelen, Marie, and Heinemann, M.: Critical Remarks on the Determination of Urinary Excretion of Ascorbic Acid, *J. Clin. Investigation* **17**: 293 (May) 1938.

23. Hawley and Stephens, Ralli, Elaine P.; Friedman, G. J., and Kaslow, M.: An Excretory Test for Vitamin C Deficiency and Subnutrition, *Proc. Soc. Exper. Biol. & Med.* **36**: 52 (Feb.) 1937. Wright, I. S.; Lilienfeld, Alfred, and MacLennan, Elizabeth: Determination of Vitamin C Saturation: A Five Hour Test After an Intravenous Test Dose, *Arch. Int. Med.* **60**: 264 (Aug.) 1937. Faulkner, J. M., and Taylor, F. H. L.: Observations on the Renal Threshold for Ascorbic Acid in Urine, *J. Clin. Investigation* **17**: 69 (Jan.) 1938.

by the Harris and Ray method⁵ on two twelve hour samples preserved with 10 per cent glacial acetic acid, and the average daily value thus obtained is considered as a blank to be deducted from the final average excretion. Test doses of from 200 to 500 mg. of ascorbic acid per day are then administered orally until saturation is reached, as shown by an excretion of at least 50 per cent of the half-day dose in twelve hours. Then follows a period of adjustment of the daily dose of ascorbic acid to the quantity required to give a titration value slightly higher than the preliminary blank value. When this dosage has been established, the same quantity is given over a final period of seven days with daily titrations of the urine to determine the average daily excretion value. The final calculation of requirement is made by subtracting from the average daily intake during the final period the average daily excretion in the same period minus the average daily excretion of the preliminary period. As the values thus obtained represent a bare equilibrium between intake and output, they may be considered as minimum requirements providing for no margin of safety.

The scheme followed by van Eekelen and her associates³⁰ consists essentially in first saturating the subject on a daily dose of 250 mg. of ascorbic acid, then depleting the reserves by a period of several weeks on a vitamin C free diet, and finally saturating again as in the first period, the end point in both being a sudden and marked increase in excretion. The total intake of ascorbic acid in the second saturation period divided by the number of days before saturation is considered as the daily use or actual requirement. Since the final period is one of saturation rather than of bare equilibrium, the values obtained represent more liberal allowances than those of Widenbauer. The method has been criticized, however,³¹ as giving entirely different results, depending on the length of the intermediate depletion period, a point which will be discussed later.

A somewhat different procedure for determining maximum or optimal requirements but also depending on saturation tests has been developed by Hauck.³² Briefly, this consists in first saturating the tissues by daily intakes of 200 mg. of ascorbic acid for six days—a period found long enough with the subjects studied to insure complete saturation as determined by the increase in excretion following a single test dose of 400 mg. The entire test is repeated two or three times to establish the individual response to the 400 mg. dose when saturation is complete. Finally a series of similar tests is run on graded doses of ascorbic acid until the least quantity is found which will induce a similar response to the test dose of 400 mg. as obtained in the preliminary tests. With the provision made in this method for complete saturation of the tissues and for individual standards of comparison, the values obtained may be considered to represent maximum requirements.

Concentration of Ascorbic Acid in the Blood.—The content of reduced ascorbic acid in fasting blood of normal subjects does not vary with age but within certain

limits is dependent on previous dietary intake of vitamin C. In the data reported in the literature³³ there appears to be rather closer agreement as to the lower than the higher limits of normality, the range extending from a minimum of about 0.6 mg. to a maximum of from 1.5 to 2 mg. or more per hundred cubic centimeters.

Abt and Farmer³⁴ have stated that "the cevitamic acid (reduced) content of the blood varies directly with the vitamin C content of the previous diet." In the opinion of Greenberg, Rinehart and Phatak,^{33b}

the estimation of the reduced plasma ascorbic acid is only a measure of the immediate nutritive or metabolic level relative to vitamin C, and is dependent on recent dietary habits to a large degree. Although it is an index of the vitamin C nutrition at the time of the test, in a single case a low level does not imply tissue injury or scurvy (either clinical or subclinical). The latter results from the operation of suboptimal or low metabolic levels over some period of time. Conversely, a good or high level would not indicate that deficiency had not operated to produce tissue injury in the past. A more accurate index of the degree of deficiency existing at the time in any given case can be had by means of serial determinations following administration of known vitamin C supplements.

Portnoy and Wilkinson³⁵ have observed occasional subnormal plasma values in subjects showing no other test for vitamin C deficiency and have suggested a similar explanation. In their opinion, however,

the finding of a normal or high plasma ascorbic acid shows the patient to have good reserves of the vitamin (always assuming that a large dose of vitamin C-containing food has not been taken before the test begins) and a single estimation should be sufficient without corroborative evidence from other tests.

Relationship Between the Ascorbic Acid Content of Blood and Urine.—A straight line relationship between the initial ascorbic acid content of the blood and the total quantity of ascorbic acid required for saturation as determined by excretion in the urine was demonstrated by van Eekelen and her associates,³⁰ who showed that with an ascorbic acid content of the blood of about 0.4 mg. per hundred cubic centimeters a total of 2 Gm. of ascorbic acid was required before saturation was reached as compared with only 1 Gm. for an initial blood value of 0.8 mg. per hundred cubic centimeters. They consider that the degree of vitamin C saturation of a subject can be estimated simply by a single blood determination in place of the tedious urinary excretion tests, a blood content of from 0 to 0.4 mg. of ascorbic acid per hundred cubic centimeters denoting a poor, from 0.4 to 0.8 mg. a moderate, from 0.8 to 1.2 mg. a very good and above 1.2 mg. an excellent state of saturation. A similar relationship was noted by Baumann,³¹ who found that with blood values as low as 0.45 mg. per hundred cubic centimeters from 20 to 40 mg. of ascorbic acid per kilogram of body weight was required

30. van Eekelen, Marie: On the Metabolism of Ascorbic Acid (Vitamin C), *Acta brev. Neerland.* 5: 165 (Dec. 14) 1935. van Eekelen, Marie; Heinemann, M., and van Wersch, H. J.: On the Daily Requirements for Ascorbic Acid of Man, *ibid.* 6: 107 (June 20) 1936. van Eekelen, Marie: On the Amount of Ascorbic Acid in Blood and Urine: The Daily Human Requirement for Ascorbic Acid, *Biochem. J.* 30: 2291 (Dec.) 1936.

31. Göthlin, G. F.; Frisell, E., and Rundquist, N.: Experimental Determinations of the Indispensable Requirements of Vitamin C (Ascorbic Acid) of the Physically Healthy Adult, *Acta med. Scandinav.* 92: 1 (June 6) 1937.

32. Hauck, Hazel M.: Unpublished data.

33. (a) Abt, A. F.; Farmer, C. J., and Epstein, I. M.: Normal Cevitamic (Ascorbic) Acid Determinations in Blood Plasma and Their Relationship to Capillary Resistance, *J. Pediatr.* 8: 1 (Jan.) 1936. (b) Taylor, F. H. L.; Chase, D., and Faulkner, J. M.: The Estimation of Reduced Ascorbic Acid in Blood Serum and Plasma, *Biochem. J.* 30: 1119 (July) 1936. (c) Degge, J. C.: Researches on the Vitamin C Content of the Blood, *Acta brev. Neerland.* 6: 64 (July 4) 1936. (d) Stephens, D. J., and Hawley, Estelle E.: The Partition of Reduced Ascorbic Acid in Blood, *J. Biol. Chem.* 115: 653 (Oct.) 1936. (e) Greenberg, L. D.; Rinehart, J. F., and Phatak, N. M.: Studies on Reduced Ascorbic Acid Content of the Blood Plasma, *Proc. Soc. Exper. Biol. & Med.* 35: 135 (Oct.) 1936. (f) Ingalls, T. H.: Studies on the Urinary Excretion and Blood Concentration of Ascorbic Acid in Infantile Scurvy, *J. Pediatr.* 10: 577 (May) 1937. (g) Pijoan, M., and Eddy, E.: Ascorbic Acid Content of Red Cells and Plasma, *J. Lab. & Clin. Med.* 22: 1227 (Sept.) 1937. (h) Baumann.³¹ (i) Sloan.³²

34. Abt, A. F., and Farmer, C. J.: Cevitamic Acid Content of the Blood Plasma, *Am. J. Dis. Child.* 54: 682 (Sept.) 1937.

35. Portnoy, B., and Wilkinson, J. F.: Vitamin C Deficiency in Peptic Ulceration and Hematemesis, *Brit. M. J.* 1: 554 (March 12) 1938.

for saturation, whereas a content of over 1.4 mg. per hundred cubic centimeters indicated a high degree of saturation.

Evidence leading to the conclusion that ascorbic acid has a definite renal threshold value at a blood concentration of about 1.4 mg. per hundred cubic centimeters has been reported by Faulkner and Taylor²³ with the conclusion that blood values at or above this level indicate saturation and below this level unsaturation in varying degree. Others believe that the threshold value varies with the person³⁶ and more particularly that there are two types of persons with high and low threshold values respectively.³⁷ This would account for the wide span which has been noted in the saturation capacity of different individuals.³⁸ Neuweiler's³⁷ evidence in support of this hypothesis is of interest also in indicating when it is safe to use blood values alone as a measure of saturation. Among the forty-three nonpregnant women whom he studied, all but one out of twelve with initial blood values ranging from 1 to 1.5 mg. per hundred cubic centimeters came within the normal four day limit of saturation, according to the Jezler and Kapp method,²¹ while all five subjects with blood values under 0.6 mg. per hundred cubic centimeters required from six to eight days to complete the test.

The remaining twenty-seven subjects with blood values decreasing from 0.95 to 0.6 mg. per hundred cubic centimeters gave inconsistent results, some completing the test within four days while others with the same initial blood values required a longer time. Neuweiler concluded that while both high and low blood values may furnish sufficient evidence of the vitamin C nutrition of a person, intermediate values of from about 0.6 to 1 mg. per hundred cubic centimeters should not be considered alone but in connection with the results of saturation tests.

Oral and intravenous tolerance tests involving simultaneous determinations of the blood and urine at frequent intervals following the administration of a single massive dose of ascorbic acid orally or intravenously have been recommended by Portnoy and Wilkinson³⁵ as furnishing the most reliable information concerning the state of vitamin C nutrition. Individual variations in the rate of absorption of ascorbic acid from the intestinal tract or possible destruction of the vitamin are considered to render the oral test somewhat less satisfactory than the intravenous tolerance test. It is suggested that in the latter method, when used as a routine, blood tests may be omitted and determinations made only of the ascorbic acid excretion during the first five hours following the injection. This abbreviated test, however, may not be valid in cases of damage to the kidneys, which is revealed by simultaneous tests on the blood and urine.³⁹

REQUIREMENTS OF VARIOUS AGE GROUPS

Infants.—The vitamin C reserves of the infant at birth depend on the state of nutrition of the mother, with umbilical cord blood usually giving higher values

than the corresponding maternal venous blood,⁴⁰ possibly because of increased use of the vitamin by the mother during labor. In a group of twenty-two hospitalized cases, Braestrup⁴¹ obtained average values of 0.26 mg. of ascorbic acid per hundred cubic centimeters for the maternal blood, 1.07 mg. for the cord blood and 0.69 mg. for capillary heel blood of the infants thirty minutes after birth. Ten days after birth these capillary blood values had dropped to an average of 0.27 mg. per hundred cubic centimeters. The mothers in this study had been on diets very deficient in vitamin C before admission to the hospital, which may account for the low value of the maternal blood.

The rapid decrease in ascorbic acid content of the blood during the first ten days, as noted, suggests that the reserves with which the infant is supplied at birth are sufficient for only a few days and that thereafter vitamin C must be supplied either through breast milk or as a supplement to artificial feeding in order to maintain the blood concentration at the level which seems indicative of a good vitamin C reserve at any age. Mindlin⁴² reports an average plasma ascorbic acid value of 1 mg. per hundred cubic centimeters for a group of about twenty infants at the age of 2 weeks, as compared with 0.3 mg. for a comparable group artificially fed from birth or for at least six days before the test, and from 0.4 to 0.8 mg. for a smaller group of artificially fed infants receiving 20, 30 or 75 mg. of ascorbic acid for a week or more, the 20 mg. dose giving as good results as the larger amounts. Braestrup⁴¹ also found that initially low blood levels could be raised to from 0.56 to 0.76 mg. per hundred cubic centimeters by a 20 mg. supplement of ascorbic acid daily but were not affected by 10 mg. These data, although fragmentary, suggest that to maintain the ascorbic acid content of the blood of artificially fed infants at low normal values during the first weeks of life not less than 20 mg. of ascorbic acid daily is needed. In Braestrup's subjects, whose weights were given, this allowance is equivalent to from 5 to 6 mg. per kilogram of body weight.

On the basis of estimates of the vitamin C intakes of breast-fed and artificially fed infants from 9 to 12 days of age excreting in twenty-four hours more than 50 per cent of test doses of 30 mg. of ascorbic acid per kilogram of body weight, injected subcutaneously, Neuweiler⁴³ also arrived at the conclusion that the vitamin C requirement of very young infants is in the vicinity of 6 mg. per kilogram of body weight and concluded that the diet of infants, especially the artificially fed, should be supplemented at this early age (less than 2 weeks) with fruit juices or a pure preparation of ascorbic acid.

In view of the fact that formerly it was considered unnecessary to supplement the diet of artificially fed infants with vitamin C before the age of 3 or 4 months and that the most recent (December 1937) recommendation of the Technical Committee on Nutrition of the

36. Lund, H.: Eine quantitative und spezifische Methode zur Ascorbinsäurebestimmung im Harn und zur Bestimmung des Schwellenwertes, *Klin. Wchnschr.* **16**: 1085 (July 31) 1937.

37. Wacholder, K., and Hamel, P.: Ueber die Vitamin C-Bilanz des Menschen: III. Taglicher Bedarf und Güte des Versorgungszustandes nach den Beziehungen des Blutgehaltes zu Ausscheidung und Gewebs-sättigung, *Klin. Wchnschr.* **16**: 1740 (Dec. 11) 1937. Neuweiler, W.: Ueber den Nachweis des Vitamin C-Sättigungsgrades des Organismus, *Ztschr. Vitaminforsch.* **7**: 128, 1938.

38. Baumann, J., and Hamel, P.: Ueber die Vitamin C-Sättigung —Kidney Retention After an Intravenous Test Dose of Ascorbic Acid, *Proc. Soc. Exper. Biol. & Med.* **35**: 55 (Feb.) 1938.

40. Abt, Farmer and Epstein,²³ Wahren, H., and Rundquist, O.: Ueber den Ascorbinsäuregehalt des Blutes von Mutter und Frucht, *Klin. Wchnschr.* **16**: 1498 (Oct. 23) 1937. Braestrup, P. W.: Studies of Latent Scurvy in Infants: 1. Capillary Resistance of Newly-Born Children and During the First Year of Life; 2. Content of Ascorbic (Cevitic) Acid in the Blood-Scrum of Women in Labour and in Children at Birth, *Acta paediat.* **19**: 320, 328, 1937. Nielsen, H. E.: Serumascorbinsyren under Normale og Forskellige Pathologiske Forhold, *Bibliot. f. Læger.* **130**: 20 (Jan.) 1938.

41. Braestrup, P. W.: Studies of Latent Scurvy in Infants: III. The Content of Reduced Ascorbic Acid in Blood Plasma in Infants, Especially at Birth and in the First Days of Life, *J. Nutrition* **16**: 363 (Oct.) 1938.

42. Mindlin, R. L.: The Relation Between Plasma Ascorbic Acid Concentration and Diet in the Newborn Infant, *J. Pediat.* **13**: 309 (Sept.) 1938.

43. Neuweiler, W.: Vitamin C—Stoffwechsel bei Neugeborenen, *Ztschr. f. Vitaminforsch.* **6**: 75 (Jan.) 1937.

Health Organization of the League of Nations⁴⁴ for the vitamin C requirement of artificially fed infants is from 5 to 15 mg. a day, what other evidence is at hand to prove or disprove this more generous allowance at an earlier age?

A condition of subacute vitamin C deficiency has been recognized⁴⁵ as occurring occasionally in infants as early as the second day of life. The condition is described as a vague nutritional upset with disturbance in water metabolism and excessive loss in weight responding promptly to treatment with ascorbic acid. Ley conducted urinary excretion tests on four male infants 4 days of age, two of whom (one breast-fed and one artificially fed) showed these symptoms of vitamin C deficiency. Although the absolute values reported are probably of no great significance, it is of interest that the excretion of ascorbic acid of the two normal infants was about twice that of the other two. The artificially fed infant was then given 50 mg. and the mother of the breast-fed infant 300 mg. of ascorbic acid daily, following which both infants showed marked clinical improvement. The urine tested after ten or twelve days had increased in volume and ascorbic acid content, and the ascorbic acid content of the breast milk had increased from 3.57 to 6.07 mg. per hundred cubic centimeters. From these and other observations, Ley concluded that there is a wide variation in the vitamin C needs of individual infants during the first few weeks of life, owing to differences in functional capacity and the oxidation processes of intermediary metabolism.

From analyses by the customary indophenol titration method of tissues and organs of infants dying at birth or at varying intervals up to the age of 4 months, Ingalls⁴⁶ has shown progressive exhaustion of vitamin C reserves with increasing age. Even more convincing evidence of the effects of lack of vitamin C in this early period of life was shown by Ingalls in the case histories and histologic sections of the bones and costochondral junctions of a small group of premature infants receiving only pasteurized mother's milk and dying before the age of 4 months. These showed unmistakable signs of vitamin C deficiency not detected during life. Accordingly, Ingalls feels that some source of vitamin C should be given as early as the first week in life. "This is particularly important for premature infants, for the artificially-fed and for those suffering from disease."

Szent-Györgi⁴⁷ once made the statement "ein optimal funktionierender Körper kann nicht durch Vitaminzufuhr verbessert werden." Later in illustrating this principle he⁴⁸ showed that while a laboratory guinea pig may be kept in a presumably satisfactory and healthy condition and be protected from outward symptoms of vitamin C deficiency on from 1.5 to 2 mg. of ascorbic acid, it requires a much larger dose for protection against diphtheria and other bacterial toxins, and in its own natural environment may consume from 20 to 40 mg. of ascorbic acid daily from green food. This quantity also represents the dose required for complete saturation of the animal's tissues. In his opinion, in the long run the physiologic quantity of any vitamin

will be found to be the amount which in its original environment the organism in question consumes daily. Applied to the vitamin C requirements of infants, this might be construed to mean the quantity of ascorbic acid furnished by the day's supply of breast milk of the best quality.

Breast milk has long been considered much richer than cow's milk in vitamin C. Chemical tests have confirmed this belief but have shown fairly wide variations in content, depending largely on the food supply of the lactating woman. (Requirements for lactation will be discussed later.) However, the range in concentration and average values reported by investigators in different countries using similar methods of titration with 2,6 dichlorophenolindophenol are surprisingly uniform.⁴⁹ The values taken as a whole show that breast milk from women on satisfactory diets may be expected to furnish from 4 to 7 or 8 mg. per hundred cubic centimeters during the first few months of lactation. In fact, a concentration below 4 mg. per hundred cubic centimeters has been considered⁵⁰ to indicate a vitamin C deficiency in the tissues of the lactating woman.

Estimates of the daily consumption of vitamin C by breast-fed infants vary according to the values selected as most representative of the average concentration of the vitamin in breast milk. Selleg and King^{49d} have estimated that under optimal conditions with a fluid intake of 21 ounces (630 cc.) an infant may receive as much as from 40 to 50 mg. of ascorbic acid daily from breast milk during the first few weeks. Widenbauer⁵¹ has reported values ranging from 18 to 78 mg. in the twenty-four hour supply of breast milk from wet nurses in different stages of lactation and at the height of saturation by the test dose method. The highest values under these conditions are, naturally, not representative of the ordinary content of ascorbic acid in breast milk. Ingalls,⁴⁶ using 4 mg. per hundred cubic centimeters as an average value, has estimated that the normal infant during the first three months of life, in consuming from 500 to 1,000 cc. of breast milk, receives the equivalent of from 20 to 40 mg. of ascorbic acid daily. Braestrup⁴¹ considers that with an average milk consumption of 150 cc. per kilogram of body weight a breast-fed infant may receive a minimum of 3 mg. and a maximum of 8 mg. of ascorbic acid per kilogram of body weight daily during the first few months of life.

None of these calculated intakes from breast milk of good quality fall below and most of them are considerably above the estimated requirements reviewed and far above the 1937 recommendation of the League of Nations Committee, as previously noted.

In spite of differences in the methods which have been used in estimating the vitamin C requirements of infants, the recommended allowances fall within the comparatively narrow range of from 5 to 8 mg. of ascorbic acid per kilogram of body weight or from 20 to 50 mg. daily after the first few days. These requirements may be met, during the first few months, by breast feeding alone under optimal conditions. How-

44. Report by Technical Commission on Nutrition on Work of the Third Session, Bull. Health Organ., League Nations 7: 475, 1938.

45. Ley, L.: Die Bedeutung des Vitamin C für das Neugeborene, Klin. Wchnschr. 16: 1425 (Oct. 9) 1937.

46. Ingalls, T. H.: Ascorbic Acid Requirements in Early Infancy, New England J. Med. 218: 872 (May 26) 1938.

47. Szent-Györgi, Albert: Die medizinische Bedeutung des Vitamins C, Deutsche med. Wchnschr. 60: 556 (April 13) 1934.

48. Szent-Györgi, Albert: Les propriétés thérapeutiques des vitamines, Presse méd. 51: 995 (June 25) 1938.

49. (a) Neuweiler, W.: Ueber den Gehalt der Frauenmilch an Vitamin C, Ztschr. f. Vitaminforsch. 4: 39 (Jan.) 1935. (b) Harris, L. J., and Ray, S. N.: Diagnosis of Vitamin-C Subnutrition by Urine Analysis, with a Note on the Antiscorbutic Value of Human Milk, Lancet 1: 71 (Jan. 12) 1935. (c) Wachholder, K.: Die Versorgung des Säuglings mit Vitamin C, Klin. Wchnschr. 15: 593 (April 25) 1936. (d) Selleg, Iva, and King, C. G.: The Vitamin C Content of Human Milk and Its Variation with Diet, J. Nutrition 11: 599 (June) 1936. (e) Widenbauer, F., and Kühner, A.: Ascorbinsäurestudien an stillenden Frauen, Ztschr. f. Vitaminforsch. 6: 50 (Jan.) 1937.

50. Baumann, T., and Rappolt, L.: Untersuchungen zum C-Vitaminstoffwechsel: II. Ueber die C-Vitaminausscheidung und den C-Vitaminbedarf laktierender Frauen, Ztschr. f. Vitaminforsch. 6: 8 (Jan.) 1937.

51. Widenbauer, F.: Der Vitamin C-Haushalt stillender Mütter, Ernährung 2: 64 (Feb.) 1937.

ever, it may be safer and more economical to supply some of the vitamin C directly to the infant rather than rely entirely on breast feeding. This practice is even more necessary for infants receiving pooled mother's milk instead of breast feeding. A 27 per cent loss of ascorbic acid was reported for samples of mother's milk held in a refrigerator for eighteen hours,^{49d} and samples of pasteurized pooled mother's milk as delivered to a hospital from a directory for mother's milk were found to contain only 0.3 mg. of ascorbic acid per hundred cubic centimeters or less than one tenth as much as fresh breast milk of average quality.⁴⁶

The ascorbic acid content of cow's milk ranges from 1 to about 2.6 mg. per hundred cubic centimeters for raw and from 0.4 to 1 mg. for pasteurized milk.⁵² The probable extent of reduction of these initial low values by the time the milk is ready for consumption by the artificially fed infant has been shown by Hawley⁵³ in analyses for ascorbic acid of samples of milk as taken from various delivery wagons to a city health bureau laboratory for bacteriologic count.

The raw milk sampled had an average ascorbic acid content of 1.65 mg., the pasteurized milk 0.9 mg. and formulas prepared from the milk for use in the hospital nursery 0.61 mg. per hundred cubic centimeters.

According to Hawley, "if non-glass cooking utensils are used in the home, even further reduction is probable. As a result the average formula of the infant (600-750 cc.) would supply only 4 to 6 mg. of vitamin C and cannot, therefore, be considered an adequate source of this vitamin."

These figures for breast milk, pooled mother's milk, and cow's milk, as modified for infant feeding, afford rather convincing evidence of the advisability of furnishing supplementary sources of vitamin C to all infants at a very early age, the need increasing from breast-fed infants to those receiving milk mixtures.

The reluctance of some physicians to recommend vitamin C supplements at an earlier age and in more generous quantities than formerly may be due in part to hesitation to apply to vitamin C the doctrine of the newer knowledge of nutrition with its distinction between the terms "adequate" and "optimal." Possibly an infant protected against the earliest detectable sign of capillary fragility may be thought to be receiving adequate vitamin C. To the physician formerly accustomed to seeing many cases of unmistakable infantile scurvy, protection against scurvy may even indicate an adequate provision of the vitamin but in neither case can the state of nutrition be considered optimal if there are no reserves to meet unexpected demands—no margin of safety.

Probably the best indication of whether or not the individual infant's need of vitamin C is being fully met is by determinations of the reduced ascorbic acid content of the blood plasma. According to Ingalls,⁴⁶ reduced values of ascorbic acid in the plasma from 2 to 1 mg. per hundred cubic centimeters indicate complete saturation, from 1 to 0.7 mg. normal, from 0.7 to 0.5 mg. low normal, from 0.5 to 0.3 mg. suboptimal, from 0.3 to 0.15 mg. asymptomatic scurvy and from 0.15 mg. to 0 scurvy. On the basis of combined saturation and blood tests conducted on a group of healthy infants and children, Chu and Sung⁵⁴ have proposed a similar

classification based on ascorbic acid values on the plasma as follows: deficiency stage 0.17-0.41 mg., pre-saturation 0.54-0.8 mg., relative saturation 0.86-1.36 mg., and postsaturation 0.85-1.25 mg. These figures are in good agreement with the standard proposed by Ingalls, based on blood values alone. It will be seen that the lowest values, 0.15 and 0.17 mg. per hundred cubic centimeters, correspond to the blood content above which, according to Göthlin, the test for capillary fragility is inapplicable. Between this "physiological minimum" and the theoretic optimal is a fairly wide range with a still indefinite end point. In Ingall's opinion "it would seem logical to suppose that saturation is the truly optimal state of ascorbic acid nutrition for the infant since in the event of an increased demand or decreased supply the vitamin depot is presumably larger than in partial saturation."

Acceptance of the theory of saturation as the optimal state involves the selection of maximum rather than minimum estimates of requirements of vitamin C. Ordinarily the additional needs of the breast-fed infant and the entire needs of the artificially fed can be met by daily allowances of orange juice, tomato juice or other fruit juices without resorting to ascorbic acid, which, however, is extremely useful in cases in which fruit juices are poorly tolerated. Of particular value to the physician or hospital dietitian in calculating the equivalent quantities of various fruit juices in terms of the day's requirement of vitamin C is the recent report of the Council on Foods⁵⁵ on the ascorbic acid content of all brands of commercially canned fruit juices accepted by the Council prior to Sept. 1, 1937. With fresh orange juice of an average ascorbic acid content of about 0.5 mg. per cubic centimeter, a 50 mg. requirement would be met by 100 cc. of the juice. In comparison with this, equivalent volumes for the various canned juices studied were: canned orange juice 110 cc., lemon juice 100 cc., grapefruit juice 125 cc., tomato juice 250 cc. and pineapple juice 350 cc. These figures are only approximate and represent a rather wide range in individual values. Furthermore, the discovery of marked differences in the ascorbic acid content of varieties and strains of tomatoes⁵⁶ may be expected to raise the average of the vitamin C content of tomato juice through the selection for the commercial manufacture of tomato juice from strains of the highest vitamin C content. At present, however, it is safe practice to use the foregoing equivalents in making a substitution for orange juice in infant feeding. In large clinics with suitable laboratory facilities an even better practice, already adopted in some hospitals, is to determine the vitamin C content of each new supply of canned fruit juices for the necessary calculations in dietary prescriptions. A study of the relative costs of various fruit juices, canned and fresh, has been reported by Hawley.⁵⁷

Children.—There have been very few reports of quantitative studies on the vitamin C requirements of healthy children. This is not surprising considering the difficulty in carrying out urinary excretion studies and the possible dangers involved in subjecting children to

52. Daniel, Esther P., and Munsell, Hazel E.: Vitamin Content of Foods, U. S. Dept. Agr., miscellaneous publication 275, June 1937, p. 175.

53. Hawley, Estelle E.: Vitamin C Content of Milks: Raw, Pasteurized and Baby Formulas, J. Am. Dietet. A. 14: 275 (April) 1938.

54. Chu, F. T., and Sung, C.: The Vitamin C Content of the Blood Plasma in Normal and Sick Children, Chinese M. J. 52: 791 (Dec.) 1937.

55. The Vitamin C Content of Commercially Canned Tomato Juice and Other Fruit Juices as Determined by Chemical Titration, Council on Foods, J. A. M. A. 110: 650 (Feb. 26) 1938.

56. MacLinn, W. A.; Fellers, C. R., and Buck, R. E.: Tomato Variety and Strain Differences in Ascorbic Acid (Vitamin C) Content, Proc. Am. Soc. Hort. Sc. 34: 543 (April) 1937. Tripp, Francis; Satterfield, G. H., and Holmes, A. D.: Varietal Differences in the Vitamin C (Ascorbic Acid) Content of Tomatoes, J. Home Econ. 20: 258 (April) 1937.

57. Hawley, Estelle E.: The Vitamin C Content of Fruit Juices, J. Am. Dietet. A. 13: 261 (Sept.) 1937.

the depletion in reserves involved in any of the test dose methods for determining requirements.

Among the subjects studied by Widenbauer,⁵⁹ using an elaborate procedure, was a healthy boy in his third year. In four out of seven tests his adjusted vitamin C consumption amounted to 22 mg., and in the other three to 21 mg. daily. These values are of special interest in terms of relative requirements, for by exactly the same methods the requirements of a grown man were 28 mg. in five tests, and 26 and 27 mg. in one test each. The very slight difference between the young child and the adult indicates that the vitamin C requirements throughout life cannot be calculated in terms of body weight alone, as was at one time suggested.¹⁸

In view of the customary use of cod liver oil or other vitamin A preparations in conjunction with orange juice in infant and child feeding, further observations on the same child are of interest. Immediately following the test period in which the consumption value of 21 mg. was established, he was given 2 tablespoonfuls of cod liver oil daily for two weeks, at the end of which time the values remained unchanged. Six months later, after a value of 22 mg. had been established, 5 cc. of the vitamin A concentrate "Vogan" was given daily for a week, after which a new test gave a value of only 9 mg. daily. These observations, which were substantiated on other subjects, suggest that vitamin A preparations at least do not increase the requirement of vitamin C and in particularly concentrated form may exert an indirect sparing action.

Three boys of preschool age (39, 57 and 59 months of age at the beginning of the experiment) served as subjects in what is perhaps the most detailed investigation of the vitamin C metabolism of young children thus far published in this country.⁶⁰ During twelve successive five day periods these children, who were kept under constant observation, were given weighed diets differing from period to period only in increasing and known amounts of vitamin C. With increasing intakes per kilogram of body weight the ascorbic acid retentions (intake minus output) were greater up to a certain point, beyond which there was no further increase with larger doses. The peaks in retention were reached at intakes of 7.5, 6.6 and 6.4 mg. per kilogram of body weight for the three subjects in the order of increasing weight. Retention values in two periods on these intakes were practically identical, 4.2, 3.8 and 3.6 and 4.1, 3.7 and 3.6 mg. per kilogram of body weight respectively. The somewhat higher intake and retention of the youngest child and the lower and almost identical values for the two older subjects are of interest in view of the difference of eighteen months between the ages of the youngest and next older, and only two months between this and the oldest child. If saturation is the criterion of optimal vitamin C nutrition, the intakes required for maximum retention might be considered as representing the vitamin C requirement of these children. Expressed as total daily intakes at the peak of retention, the average values in round numbers were 117, 121 and 120 mg. respectively. At this point the urinary excretion of vitamin C by two of the subjects exceeded and of the other very nearly equaled 50 per cent of the intake, another criterion of saturation.

There is a wide range between the Widenbauer figures of 20 and 21 mg. of ascorbic acid as the daily requirement of a child in his third year and the maxi-

mum retention or saturation values of from 117 to 123 mg. for children from 3 to 5 years of age, as calculated from these data of Everson and Daniels. Although the higher values seem unpractical if considered in terms of orange juice alone, 2 cc. of which is usually required to furnish 1 mg. of ascorbic acid, a considerable proportion of the total intake of ascorbic acid in these experiments was furnished by other foods—as would be the case in ordinary, well planned diets for growing children. In the particular diets on which maximum retentions were secured on the two extremes of intake, 116.7 and 122.8 mg. respectively, orange juice furnished 96 and 90 mg. of the total, requiring about 6½ and 6 ounces (195 and 180 cc.) respectively. While this is a considerably larger volume than the customary allowance for children, it is evidently not beyond the capacity of the preschool child.

Other studies dealing with the vitamin C metabolism of children⁵⁹ represent, for the most part, hospitalized patients and are of doubtful value in an estimation of the requirements of normal healthy children although of interest in showing the increased use or wastage of vitamin C in certain diseases.

The studies of Abt, Farmer and Epstein^{33a} and of Ingalls^{33f} have shown the constancy of the ascorbic acid content of blood plasma of normal subjects at different ages and the validity of applying to children the standards previously noted. Attention has already been called to the shortened procedure recommended by Harris and Abbasy²⁴ for routine surveys of school children. In attempting to set up a "normal minimal" standard of urinary output of ascorbic acid more adapted to children than the 13 mg. standard of Harris, Bumbalo⁶⁰ found that the excretion was directly dependent on the intake and showed no constancy from subject to subject. Among sixteen healthy children from 5 to 13 years of age, the twenty-four hour ascorbic acid excretion ranged from 11 mg. for a boy aged 13 years whose daily diet included a glass of orange juice (about 60 cc.) to 71 mg. for a girl aged 5 years consuming four or five large oranges daily. The average daily excretion for the group was approximately 28 mg. as compared with about 8 mg. for the same number of tuberculous children in the same age range. Baumann and Rappolt⁶¹ consider that a child is in a state of vitamin C saturation if more than 80 per cent of a test dose of 100 mg. of ascorbic acid administered orally is excreted within twenty-four hours; if the excretion is between 80 and 40 per cent, a slight deficiency, and under 40 per cent a marked deficiency is indicated.

Accumulated observations by these methods and further studies of the concentration of ascorbic acid in the blood of children on diets of known ascorbic acid content should afford a better basis for estimating the vitamin C requirements of children. Meantime the chief and perhaps the only valid arguments against great liberality in vitamin C allowances for young chil-

59. Harris, Abbasy and Yudkin.¹⁹ Sendroy, J., Jr., and Schultz, M. P.: Studies of Ascorbic Acid and Rheumatic Fever: I. Quantitative Index of Ascorbic Acid Utilization in Human Beings and Its Application to the Study of Rheumatic Fever, *J. Clin. Investigation* 15: 369 (July) 1936. Schultz, M. P.: Studies of Ascorbic Acid and Rheumatic Fever: II. Test of Prophylactic and Therapeutic Action of Ascorbic Acid, *ibid.* 15: 385 (July) 1936. Abbasy, M. A.; Hill, N. G., and Harris, L. J.: Vitamin C and Juvenile Rheumatism, with Some Observations on the Vitamin-C Reserves in Surgical Tuberculosis, *Lancet* 2: 1413 (Dec. 12) 1936. Abbasy, M. A.; Harris, L. J., and Gray Hill, N.: Excretion of Vitamin C in Osteomyelitis, *ibid.* 2: 177 (July 24) 1937. Keith, J. D., and Hickmans, Evelyn M.: Vitamin C Excretion in Children with Particular Reference to Rheumatic Fever, *Arch. Dis. Child.* 12: 125 (June) 1937. 60. Bumbalo, T. S.: Urinary Output of Vitamin C of Normal and of Sick Children, *Am. J. Dis. Child.* 55: 1212 (June) 1938. 61. Baumann, T., and Rappolt, L.: Untersuchungen zum C-Vitaminstoffwechsel: 3. Ueber den C-Vitaminstoffwechsel bei Kindern, *Ztschr. Vitaminforsch.* 6: 24 (Jan.) 1937.

58. Everson, Gladys J., and Daniels, Amy L.: Vitamin C Studies with Children of Preschool Age, *J. Nutrition* 12: 15 (July 10) 1936.

dren are the relatively high cost of orange juice and equivalent quantities of tomato juice and other fruit juices, and the possible, although exceptional, danger of acquiring a sensitivity to these juices through unusually high intakes. For older children with a greatly increased variety of foods furnishing appreciable quantities of vitamin C it is possible to provide a liberal amount of the vitamin even in low cost diets. As a final word in favor of liberal allowances, a statement by Chapin⁶² at a round table discussion at the 1937 meeting of the American Academy of Pediatrics may be quoted: "Apparently the minimum amount [of vitamin C] needed to prevent scurvy is only a fraction of the desired amount for optimal health. So far as is known, it has never been possible to produce toxic symptoms by giving large doses of vitamin C."

Adults.—Göthlin's earliest investigation of the physiologically indispensable requirements of vitamin C, as determined by tests for capillary fragility² has been repeated by Göthlin and his associates⁶¹ with the use of ascorbic acid in place of orange juice and a mixed diet estimated to furnish only 2 mg. of ascorbic acid per person daily in place of the liquid diet of the earlier study. The subjects were again physically healthy schizophrenic adults, two males and two females, having normal gastric secretion of hydrochloric acid, blood sedimentation rate and capillary resistance. The experiment required from six to eight months for completion. At the point of final restoration to normal of the lowered capillary resistance the intakes of ascorbic acid, corrected by the addition of 2 mg. for the ascorbic acid content of the diet amounted to 0.39, 0.43, 0.44 and 0.48 mg. per kilogram of body weight for the four subjects respectively, representing a range of from 23.4 to 28.8 mg. for the total daily requirement of an adult weighing 60 Kg. These values are in surprisingly close agreement with the earlier estimates of from 21 to 30 mg. as calculated from the orange juice required in Göthlin's first experiments and of from 19 to 27 mg. as estimated from guinea pig requirements for the same degree of protection. Commenting on these values as related to dietary recommendations, the authors state:

It will be realized that the daily supply should be more generous than the figures indicate. The supply should no more be limited to what has proved to be the indispensable minimum than the supply of protein in the dietary for man should be limited to the minimum intake sufficient to maintain nitrogen balance.

However, no estimate is given for the lower limit of optimal daily intake on the ground that any investigation of this question

should take into consideration the circumstance that the supply of vitamin C which has been usual for generations is, owing to differences in obtainable food material and consequently in diet, entirely different for the people who live in different latitudes, a circumstance which may also possibly have affected their vitamin requirements.

It is significant that by an entirely different method, but one which may also be interpreted as yielding minimum rather than optimal values, Widenbauer²⁹ obtained values of about 28 mg. as his own daily requirement over a total period of 210 days and that of a nonpregnant woman. As no account was taken of the vitamin C content of the diet, which was low but not absolutely free from ascorbic acid, the actual con-

sumption of vitamin C was undoubtedly somewhat higher than the figures given.

In experiments conducted by van Eekelen³⁰ on herself following the method previously outlined, which may be expected to give higher values than either the Göthlin or the Widenbauer method, the requirement or "daily use" of ascorbic acid amounted to 34 mg. after a depletion period of ninety-four days and to 63 mg. after a period of only twenty-seven days. In van Eekelen's opinion, the daily requirement of ascorbic acid is adapted to the existing storage of the vitamin. If the diet is customarily low in vitamin C or if, as in the case of some of her experiments, there has been a prolonged depletion period, the requirement or "daily use" of the vitamin is lower than if the diet has been richer in the vitamin or there has been only a short depletion period. The selection of the upper value (63 mg.) as her daily requirement was presumably based on a consideration of her customary dietary habits. The same idea of decreased requirements with prolonged subsistence on diets low in vitamin C has been brought out by Wachholder,⁶³ who also considers it unwise to recommend the lowest values that may be obtained because they provide no margin of safety for increased use of the vitamin in infections and for the possible increased requirements of muscular work either in manual labor or in exhaustive sports.

With due recognition of the influence of the past dietary history on vitamin C requirements, a factor also recognized by Göthlin as already noted, the van Eekelen method still seems lacking in precision. Göthlin⁶¹ has criticized the indefiniteness in the end point of the test as follows:

Without an objective reason for deciding the duration of the period of abstinence, it appears that every preconceived view as to the requirements of ascorbic acid in man could find confirmation by means of an investigation in accordance with van Eekelen's principle provided that the length of the period of abstinence is adapted to suit the preconceived view.

In two other studies by essentially the same method⁶⁴ requirement values were obtained for four adult subjects equivalent to 0.70, 0.78, 0.83 and 0.83 mg. respectively per kilogram of body weight. For the adult weighing 60 Kg. the range in total daily requirement is from 42 to 50 mg., or nearly twice as much as the indispensable minimum requirement, whether determined by the Göthlin test for capillary fragility or by the saturation method of Widenbauer.

The saturation method employed by Hauck has not yet been tested on a sufficient number of subjects to warrant definite conclusions, but preliminary results are of considerable interest. For the six subjects (college graduate students and faculty) on whom at least three separate preliminary saturation tests had been made at the time of writing, the average responses in urinary excretion of ascorbic acid to a 400 mg. test dose administered after the subjects had received 200 mg. of ascorbic acid daily for six days in addition to the vitamin C furnished by a diet not absolutely free from vitamin C ranged from 229 to 274 mg. with two of the

63. Wachholder, K.: Ueber die Vitamin C-Bilanz des Menschen: IV. Einschränkung des Bedarfes bei mangelhafter Zufuhr und deren ernährungsphysiologische Bedeutung. *Klin. Wchnschr.* 17:5 (Jan. 1) 1938.

64. van Wersch, H. J.: Determinations of the Daily Requirements for Ascorbic Acid of Man, *Acta brev. neerland.* 6:86 (July 4) 1936. Heinemann, M.: On Human Requirements for Vitamin C Under Different Conditions, *ibid.* 6:144 (Oct. 15) 1936. Heinemann, M.: 1. On the Relation Between Diet and Urinary Output of Thiosulfate (and Ascorbic Acid); 2. Human Requirements for Vitamin C, *Biochem. J.* 30:2292 (Dec.) 1936.

62. Chapin, H. D.: Vitamins C and D (in Round Table Discussion on Vitamins), *J. Pediat.* 12:529 (April) 1938.

subjects giving no individual response above 249 mg. and two none lower than 240 mg. These values afford another illustration of differences in the saturation or retention capacities of different individuals. In four subjects for whom fairly clearcut results were obtained in the final adjustment in dosage of ascorbic acid to the smallest amount producing excretion values comparable to the individual standards established in the preliminary tests, the estimated requirements were equivalent to 1.18, 1.24, 1.33 and 1.62 mg. per kilogram of body weight or from a little over 70 to nearly 100 mg. as the daily requirement for maintaining complete saturation in an adult weighing 60 Kg.

Thus for adults as well as for infants and children the range of estimated requirements from the physiologically indispensable minimum to complete saturation is extremely wide—from 25 or 30 mg. daily or from about 0.4 to 1.6 mg. per kilogram of body weight—a fourfold increase from the absolute minimum to what might be called *luxus* consumption. Whatever may be the uncertainty about the upper limits of requirement, there seems no doubt that the requirement of 30 mg., as adopted by the Technical Commission on Nutrition of the Health Organization of the League of Nations,⁴⁴ should be considered only as the minimum for protection against scurvy and not as the requirement for satisfactory nutrition. For this even the frequently recommended allowance of 50 mg. should probably be considered as the barely adequate rather than the optimal requirement, with considerably larger quantities desirable when economically possible. There is some indication that a particularly generous margin of safety should be the rule in allowances of vitamin C for old people.⁶⁵ As will be noted in the following section, pregnant and lactating women should have at least twice as much vitamin C as would meet the ordinary requirements of nonpregnant women.

A report from the Massachusetts and Rhode Island state colleges⁶⁶ covers urinary excretion studies on more than 200 freshmen and forty junior women students. The Massachusetts subjects included two groups of about seventy students each tested at the beginning and near the close of their first year at college and the Rhode Island subjects about sixty freshmen and forty juniors tested the same year. The range in the "resting level" of urinary ascorbic acid was very wide in each group but strikingly similar for the three groups of freshmen students as reflected in the graphic array of individual figures and also in values of 15 mg. (Rhode Island), 20 mg. (Massachusetts, 1936) and 22 mg. (Massachusetts, 1937) representing the average daily excretion of ascorbic acid of the subjects in each group. Corresponding averages for the Rhode Island juniors and practically the same groups of Massachusetts students tested in the spring of their freshman year were 28, 33 and 27 mg. respectively. These higher averages as well as decidedly higher values for some of the individual students suggest aroused interest in the selection of foods of higher intake of vitamin C as the result of individual or group instruction.

In the first period in the aforementioned study about 70 per cent of the Massachusetts and 85 per cent of the Rhode Island students had excretion values of 20 mg. or less, while in the second period this figure dropped

to 46 and 47 per cent for the Massachusetts subjects and 50 per cent for the Rhode Island juniors. Unpublished data from comparable studies with even greater uniformity in technic on groups of students at the state colleges of Montana, Oregon, Washington and Utah⁶⁷ show a similar wide range in individual values. Rough calculations indicate that excretion values of 20 mg. or less were the rule in about 33 per cent of the Montana, 35 per cent of the Oregon, 30 per cent of the Utah and 32 per cent of the Washington group. If there is any significance in the statement of the Harris group¹⁹ that an excretion of 20 mg. indicates a moderately low intake of vitamin C, it would seem that about one third of the young women college students in the Northwest and about three fourths of similar students in the Northeast with no particular dietary instruction were on a none too liberal vitamin C intake.

In these cooperative studies smaller numbers of subjects are being given saturation tests, and an effort is also being made to correlate the estimated vitamin C content of the individual diets with the excretion values, but information is not yet available on these points.

Pregnant and Lactating Women.—All evidence points to a greatly increased need of vitamin C in pregnancy, which continues through the lactation period. In the investigation of Widenbauer,²⁹ to which frequent reference has been made because of the comparative value of his data, a nonpregnant woman with a minimum requirement or "daily use" of 28 mg. was found to need 71 mg. in the third and 67 mg. in the eighth month of pregnancy. The slight drop in the later period may not be significant, but the two values in comparison with the nonpregnant value indicate a more than doubled requirement during pregnancy. Following the same method with a group of healthy women in the eighth and ninth months of pregnancy, Gaechtgens⁶⁸ obtained the rather wide range in values of from 33 to 64 mg. and recommended not less than 100 mg. daily as a safe requirement for pregnancy. As his values were obtained by a method which gives only about 28 mg. as the ordinary adult requirement, the additional allowance for pregnancy is very generous. In Gaechtgens' opinion, the increased vitamin C requirement during pregnancy is due not to increased metabolism but to the fetal and placental requirements for storage. Evidence of increased requirements during pregnancy has also been shown by Neuweiler⁶⁹ in urinary excretion tests following the intravenous injection of 200 mg. of ascorbic acid. More than half of a group of apparently healthy pregnant women were found by Gaechtgens and Werner⁷⁰ to have a significant saturation deficit as indicated by the increased length of time required for saturation according to the Jezler and Kapp criteria.²¹

It is obvious that the nursing mother needs enough vitamin C to meet her own requirements and to maintain a satisfactory concentration of the vitamin in her milk. The various studies on the requirements of vitamin C during lactation⁷¹ have shown that under favor-

67. Richardson, Jessie E.; Fincke, Margaret L.; Todhunter, E. Neige, and Brown, Almeda P.: Personal communications to the author.

68. Gaechtgens, G.: Der Tagesverbrauch an Vitamin C in der Schwangerschaft, *Arch. f. Gynäk.* 164: 571 (Aug. 26) 1937.

69. Neuweiler, W.: Ueber den Bedarf an Vitamin C während Gravidität und Lactation, *Klin. Wchnschr.* 14: 1793 (Dec. 14) 1935.

70. (a) Gaechtgens, G., and Werner, E.: Das Vitamin C-Defizit in der Gravidität, *Arch. f. Gynäk.* 163: 475 (March 5) 1937; (b) Zur Frage des Vitamin C-Defizits in der Gravidität und während der Lactation, *Klin. Wchnschr.* 16: 843 (June 12) 1937.

71. Neuweiler.⁶⁹ Chu, F. T., and Sung, C.: Effect of Vitamin C Administration on Vitamin C of Milk and Urine of Lactating Mothers, *Proc. Soc. Exper. Biol. & Med.* 35: 171 (Oct.) 1936. Widenbauer and Kühner.²⁹ Baumann and Rappolt.²² Gaechtgens and Werner.⁷⁰

65. Harris, Abbasy and Yudkin.¹⁹ Gander and Niederberger.²⁷
66. Mitchell, Helen S.; Merriam, Oceana A., and Batchelder, Esther L.: The Vitamin C Status of College Women as Determined by Urinary Excretion, *J. Home Econ.*, to be published.

able conditions breast milk can be enriched to values considerably above the average but that there is an upper limit which cannot be exceeded. As Baumann⁷² has expressed it, there is no lower threshold for the secretion of ascorbic acid from the blood into the milk and the process may go on until the maternal organism is greatly depleted, but there is an upper limit of concentration at about 8 mg. per hundred cubic centimeters of milk. Conversely, there is no upper limit of excretion of ascorbic acid in the urine but a lower one of about 0.1 to 0.14 mg. per hundred cubic centimeters of blood. Baumann and Rappolt⁵⁰ have calculated that for a milk production of 800 cc. a day with an ascorbic acid content of at least 5 mg. per hundred cubic centimeters at least 50 mg. of ascorbic acid should be added to the daily requirement of the nonpregnant woman.

A distinction has been pointed out by Gaeltgens and Werner⁷³ between the effects of a deficiency of vitamin C in pregnancy and in lactation. When the requirements are not met during gestation, the maternal organism becomes depleted at the expense of the fetus; whereas in lactation the maternal organism is protected and the infant suffers through decreased content of ascorbic acid in the milk. If this theory is sound, it would seem advisable to be more insistent on recommending a greatly increased intake of vitamin C during pregnancy than in lactation and rely more in the latter period on supplementing the probable deficiencies in the breast milk by giving orange juice or other easily taken and readily assimilable sources of vitamin C directly to the infant at a very early age. However, no harm and undoubtedly much benefit will accrue to the nursing mother if her vitamin allowance is doubled during the period of considerable drain on her reserves.

FACTORS AFFECTING REQUIREMENTS OF VITAMIN C

While it is beyond the scope of this paper to discuss the requirements of vitamin C in illness, and the studies that have been reviewed in an attempt to arrive at some decision concerning requirements have been confined to those dealing with presumably physiologically healthy subjects, no greater argument can be given in support of liberality in allowances than to call attention to the increased use or disappearance of ascorbic acid which has been observed under various conditions of heightened metabolic activity such as heavy manual labor or violent exercise²⁵ and in certain febrile conditions, notably tuberculosis.⁷⁴ In fact it has even been suggested that ascorbic acid metabolism may be an index of total metabolism and thus serve as a general diagnostic guide.

VITAMIN C IN HUMAN DIETS

With the ascorbic acid content of any individual food in its natural state varying as widely as has been shown in two recent critical compilations of the literature,⁷⁵ and with the uncertain losses that may occur in such foods before their final consumption, it has seemed useless to attempt to estimate requirements from records of food consumed by groups of presumably healthy per-

sons of different ages, nor can such records be expected to give accurate data as to the actual consumption of ascorbic acid in comparison with estimated requirements. It is, nevertheless, of some interest, as indicating trends in consumption, to study the accompanying table, a companion to the one presented for vitamin A in a previous paper of this series.⁷⁶ With all due allowance for the sources of error in such calculations, it is of significance that as the weekly expenditure for food increased the estimated ascorbic acid content of the diet increased almost without exception. When it is considered that in the low cost diets the proportion of ascorbic acid furnished by orange juice was probably much less than in diets of higher cost and that consequently a greater deduction should be made for losses of the vitamin before consumption, it will be seen that certainly the

*Estimated Ascorbic Acid Content of Diets of Families Not on Relief, 1935-1936 (in Milligrams per Requirement Unit)**

Region and Degree of Urbanization	Average† in Milligrams per Adult per Day‡ for Families Spending§ Weekly per Head for Food					
	\$1.25-\$1.57	\$1.58-\$2.49	\$2.50-\$3.12	\$3.13-\$3.74	\$3.75-\$4.37	
City¶						
North Atlantic.....	40.0	57.5	70.0	87.5	97.5	
East North Central.....	47.5	57.5	75.0	77.5	107.5	
East South Central.....	50.0	67.5	85.0	
Pacific.....	70.0	77.5	95.0	107.5	115.0	
Village#						
North Central.....	40.0	57.5	77.5	77.5	
Southeast.....	40.0	52.5	72.5	95.0	92.5	
Pacific.....	50.0	77.5	87.5	165.0	100.0	
Farm¶						
North Central.....	66.5	70.0	90.0	100.0	
Southeast.....	55.0	70.0	80.0	
Pacific.....	83.5	106.0	

* Data furnished by Dr. Hazel K. Stiebeling, Senior Food Economist, Bureau of Home Economics, U. S. Department of Agriculture.

† These averages represent the value of the uncooked food. They are higher, therefore, than the value of food actually eaten.

‡ The following scale of family coefficients was employed in evaluating the ascorbic acid intake for families of different types in terms of an adult:

Adults, 20 years and over.....	1.0
Boys 16-19 years.....	1.2
Boys 13-15 years.....	1.0
Boys 11-12 years, girls 14-19 years.....	0.9
Boys 9-10 years, girls 11-13 years.....	0.8
Boys 4-8 years, girls 4-10 years.....	0.7
Children under 4 years.....	0.7

§ Adjusted to 1933 retail price levels.

¶ Families of employed workers. Field work conducted by the U. S. Bureau of Labor Statistics.

All occupational groups.

¶ Farm operators; farm-furnished food valued at farm prices.

lowest cost diet, and probably the next higher (except for the farm group) furnished less than a safe allowance of vitamin C and that only in the two highest cost groups could the intake be considered to represent a very generous allowance.

A point of interest is the consistently higher ascorbic acid content of the diets at all cost levels in the Pacific than in the North Atlantic region for the city families, the only group for which data are reported for both of these regions. These differences are brought out even more strikingly in the detailed report on the diets of families of employed wage earners and clerical workers in cities.⁷⁷ As many as 45 per cent of these families in the North Atlantic region bought foods supplying less than 37.5 mg. of ascorbic acid per requirement unit a day, whereas none of the Pacific city families had diets

72. Baumann, T.: Untersuchungen über den C-Vitaminstoffwechsel bei laktierenden Frauen und über den Grad der physiologischen und pathologischen C-Vitaminsättigung des menschlichen Organismus, *Jahrb. f. Kinderh.* 150: 193, 1937; *Nutrition Abstr. & Rev.* 7: 1083, 1937.

73. Gaeltgens, G., and Werner, E.: Vitamin C-Belastungen bei Stillenden Wöchnerinnen, *Arch. f. Gynäk.* 165: 63, 1937.

74. Martin, G. J., and Heise, F. H.: Vitamin C Nutrition in Pulmonary Tuberculosis, *Am. J. Digest. Dis. & Nutrition* 4: 368 (Aug.) 1937.

75. Daniel and Munsell,²² Boas Fixsen, Margaret A., and Roscoe, Margaret H.: Tables of the Vitamin Content of Human and Animal Foods, *Nutrition Abstr. & Rev.* 7: 523 (April) 1935.

76. Beeher, Lela E.: Vitamin A Requirements and Practical Recommendations for Vitamin A Intake, *J. A. M. A.* 110: 1920 (June 4) 1938.

77. Stiebeling, Hazel K., and Phipard, Esther L.: Diets of Families of Employed Wage Earners and Clerical Workers in Cities, U. S. Dept. Agr. Circ. 507, 1938.

so low in vitamin C. With expenditures for food ranging from \$2.50 to \$3.12 per person weekly, considered representative of the moderately well-to-do, about 37 per cent of the families in the North Atlantic group and 70 per cent in the Pacific group bought food furnishing more than 75 mg. of ascorbic acid (uncorrected) a day. These figures are entirely consistent with the urinary excretion data for groups of college women in these areas for, as noted earlier, low excretion values for ascorbic acid (presumably indicative of low intake) were the case in from 75 to 80 per cent of the North Atlantic group and from 30 to 35 per cent in the Pacific group.

SUMMARY AND CONCLUSIONS

A positive statement of human requirements is difficult to make because of uncertain or unsatisfactory methods for its determination in the living organism, lack of agreement as to the most satisfactory state of nutrition with respect to this vitamin and individual differences in requirements.

Based on the methods that have been followed, three levels of requirement may be considered in terms of the minimum quantities of ascorbic acid required: (1) to prevent the slightest decrease in capillary resistance or to maintain uniform excretion of the vitamin barely above that on a vitamin C-free diet; (2) to maintain uniform excretion after a depletion period following a preliminary saturation period, and (3) to maintain the tissues in a state of saturation as determined by various modifications of the test dose method. These levels of requirement may conveniently be termed the physiologically indispensable, adequate, and saturation or luxus consumption values respectively.

The estimated requirements for various age groups as reviewed lie within the following limits of absolute values: infants, from about 8 mg. (newly born) to 50 mg. daily; children, from 22 to 100 mg. or more; adults, from 28 to 100 mg. or more. With due allowance for unlike methods followed in their determination, these values may be considered to represent roughly the range from the physiologically indispensable minimum to saturation or luxus consumption. Values of about 20 mg. daily for infants, 40 mg. for children and from 50 to 60 mg. for adults may be considered as tentative estimates for the middle or barely adequate consumption level, with but little margin of safety or allowance for individual variations in requirement.

Requirements have also been estimated in terms of body weight: infants from 3 to 8 mg., children from 6.4 to 7.5 mg. and adults from 0.7 to 1.6 mg. per kilogram of body weight. While the data are far too incomplete to warrant separation of these values into the three levels or to permit of definite conclusions concerning the rate of decrease in requirement per unit weight with increasing age, a comparison of the absolute and relative values for different ages suggests that vitamin C requirements are related both to body weight and to metabolic rate, the effect of the latter being the more pronounced.

It has been stated that "saturation is the truly optimal state of ascorbic acid nutrition for the infant since in the event of an increased demand or decreased supply, the vitamin depot is presumably larger than in partial saturation."^{33f} The same argument would seem to be valid for the growing child. Since vitamin C is intimately concerned with cellular metabolism, liberality in allowance throughout the entire period of growth seems logical. There is still considerable difference of opinion

concerning the satisfactory allowance for the adult. While it may be safe to accept the middle level of requirement, the upper level of luxus consumption is more in keeping with the policy of providing a generous margin of safety in most dietary allowances. In pregnancy and lactation with their increased demands, the margin of safety afforded by the upper level of requirement is most essential, and this may also hold for elderly persons.

Council on Pharmacy and Chemistry

REPORT OF THE COUNCIL

THE COUNCIL HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORT. IN ADDITION THE COUNCIL VOTED TO INCLUDE IMMUNE GLOBULIN (HUMAN) IN N. N. R. AND TO ACCEPT CERTAIN SUBMITTED BRANDS. THE MONOGRAPH AND THE DESCRIPTION OF ACCEPTED PRODUCTS APPEARS IN THIS DEPARTMENT OF THIS ISSUE OF THE JOURNAL.

PAUL NICHOLAS LEECH, Secretary.

THE PRESENT STATUS OF IMMUNE GLOBULIN (HUMAN)

The Council issued a preliminary report on Immune Globulin (Human) and two submitted brands—Placimmunin-Squibb and Immune Globulin (Human)-Lederle. This report appeared in THE JOURNAL for Aug. 17, 1935,¹ along with an editorial summarizing the report.² The conclusion of the report, which was based principally on McKhann's work,³ read as follows:

"After considering the available evidence, the Council decided that although Immune Globulin (Human) appears to be a promising immunizing agent, more evidence of its value is needed before it may be generally used by the medical profession.

"The Council, therefore, postponed consideration of Immune Globulin (Human) and the brands submitted by Squibb (Placimmunin) and Lederle until such further evidence is available, and authorized publication of the foregoing report."

Subsequently the National Drug Company presented its brand of immune globulin (human). Many additional references have appeared in the literature in the two years since the publication of the previous report and it is therefore essential to consider the present literature.

VARIOUS ANTITOXINS CONTAINED IN IMMUNE GLOBULIN (HUMAN) AND THEIR RELATIONSHIP TO TESTING ITS POTENCY

Karelitz⁴ concluded from a series of experiments that the protein extract composed of globulins derived from the human placenta contained diphtheria and scarlet fever antitoxins, antibodies which neutralize the virus of acute anterior poliomyelitis and protect exposed susceptible children against measles.

Eley⁵ noted that placental extracts had been found to prevent or modify measles in nonimmune individuals who had been infected by the virus; that it neutralized diphtheria toxins; that it blanchied scarlet fever reactions and neutralized the virus of poliomyelitis. He also noted that McKhann⁶ had determined that the substances antagonistic to the viruses of measles and poliomyelitis were present in all his globulin fractions, whereas the antibodies for scarlet fever and diphtheria were found only in the more soluble pseudoglobulins.

1. Preliminary Report of the Council: Immune Globulin (Human): Placimmunin-Squibb and Immune Globulin (Human)-Lederle, J. A. M. A. 105: 510 (Aug. 17) 1935.

2. Immune Globulin (Human) and Measles, editorial, J. A. M. A. 105: 514 (Aug. 17) 1935.

3. McKhann, C. F., and Chu, F. T.: Antibodies in Placental Extracts, J. Infect. Dis. 52: 268 (March-April) 1933. Schick, Bela, and Karelitz, Samuel: Studies in Prophylaxis of Measles, Am. J. Dis. Child. 47: 1162 (May) 1934. McKhann, C. F., and Chu, F. T.: Use of Placental Extract in the Prevention and Modification of Measles, Am. J. Dis. Child. 45: 475 (March) 1933. McKhann, C. F., and Coady, Harriet: Immunity in Infants to Infectious Diseases: Placental Antibodies, South. M. J. 27: 20 (Jan.) 1934. McKhann: Totals in table 3 (not published elsewhere).

4. Karelitz, Samuel: Measles Prophylaxis, New York State J. Med. 35: 376 (Sept. 1) 1935.

5. Eley, R. C.: Placental Extract (Immune Globulin Human) with Especial Reference to Its Use in Prevention and Modification of Measles, J. Michigan M. Soc. 35: 769 (Dec.) 1936.

6. McKhann, C. F.; Green, A. A., and Coady, Harriet: Factors Influencing Effectiveness of Placental Extract in Prevention and Modification of Measles, J. Pediat. 6: 603 (May) 1935.

Karelitz, Greenwald and Klein⁷ noted that the prophylactic value of this substance could not be reliably determined by its nitrogen content and that McKhann's studies had indicated that this substance, which was extracted from the human placenta, contained antibodies for measles and for diphtheria. Karelitz and his associates noted that for all practical purposes the globulin had been shown to be as effective as blood serum used for the same purpose. They concluded that the immunizing value of the amount of maternal blood serum which contains one unit of diphtheria antitoxin should be equivalent to the amount of immune globulin which contains one unit of diphtheria antitoxin. They tested this hypothesis by adjusting the amount of immune globulin used in immunizing their patient on the basis of the diphtheria antitoxin titer. As a result their dosage varied from 3.7 to 20 cc. in obtaining results similar to those obtained by administering 10 cc. of adult serum. They suggested the application of this method to the evaluation of various lots of immune globulin expressed from the placenta.

Karelitz and Greenwald⁸ studied the possible source of the antibodies which these placental extracts contained. They expressed the belief that the immunizing properties of the placental fluid (extracellular constituents of the placenta) was actually comparable to that of the blood serum. They compared the antitoxic titer of maternal circulating blood with the serum extracted from the placenta and concluded from their studies that the activity of the globulin which was obtained from the placental fluid could be tested as accurately against the fluid as against the maternal circulating blood.

THE IMMUNITY PRODUCED BY MODIFIED MEASLES

In considering a preparation which is proposed primarily for the purpose of modifying a disease, it is well to study the degree and extent of the immunity which results from such modified disease in comparison with the immunity following an unmodified case of the same disease.

Townsend⁹ made a special study of this particular question. He instituted a ten year follow-up on a series of thirty-two patients given 9 cc. of convalescent whole blood for the prevention of spread of a measles epidemic in a boarding school. None of the thirty-two developed measles during the subsequent ten year period. Nine of them gave a definite history of exposure and five others a questionable history of exposure (in the presence of an epidemic without any direct known contact). The author concluded that there was no evidence that the immunity conferred by modified measles (in this series with convalescent whole blood—not immune globulin) was any less than that which followed unmodified measles.

McKhann⁶ found that the immunity which followed the prevention of measles by the injection of immune globulin was passive in type and of short duration. For that reason he did not believe that the preparation should be used for that purpose except in institutions, for small infants and for those suffering from other illnesses. He noted that it remains to be determined to what degree measles can be modified and still permit the development of a permanent immunity. Ordinarily it is considered that permanent immunity usually follows the modified as well as the unmodified disease. It is granted that it is important to note that the permanence of immunization has not been determined. Nevertheless, the agent appears to be as useful as other immunizing agents employed to modify or prevent the disease.

IMMUNE GLOBULIN (HUMAN) AND OTHER IMMUNIZING AGENTS

Karelitz,⁴ after an extensive review of the literature and study of his own cases, concluded that the therapy of choice in the prevention of measles was convalescent serum; that adult blood and serum were effective and practicable; that placental extract was effective, but that reactions were sometimes severe and that the proper dosage must be accurately determined in order to obtain the desired results. He included in his work table 1.

7. Karelitz, Samuel; Greenwald, C. K., and Klein, A. J.: A Method of Determining Dosage of Placental Globulin in Measles Prophylaxis, *Proc. Soc. Exper. Biol. & Med.* **32**: 1359 (May) 1935.
8. Karelitz, Samuel, and Greenwald, C. K.: Comparison of Maternal Circulating Blood Immunity with that of Placental Fluid, *Proc. Soc. Exper. Biol. & Med.* **32**: 1362 (May) 1935.
9. Townsend, J. H.: Does Modified Measles Confer Lasting Immunity? *New England J. Med.* **214**: 732 (April 9) 1936.

The results noted in this table indicate that there is little difference between the three agents employed, provided they are properly standardized and administered on the basis of the standardization.

Blackler¹⁰ used adult immune serum in the immunization of 105 patients, twelve of whom developed "full-blown" measles (all these twelve patients were given the serum of the same donor). Eight developed modified measles, five of these from the donor referred to and eighty-five were entirely protected by the use of this serum, which was obtained from patients giving a definite history (with the exception of the donor mentioned) of measles.

Eley⁵ noted that the effectiveness of immune globulin as it is employed in the immunization of measles depended on the dosage, potency, the type of exposure, the time element, the age and the size of the patient. He further noted that the desirability of protection or modification depended on the circumstances; that modification is desirable in most home cases provided the children were not too young to be exposed to even a mild case of measles; that absolute prevention was essential, in the control of measles in hospitals and institutions. He reviewed the literature and concluded that the evidence indicated that it was a valuable preparation in the prevention or modification of measles but that its use as an immunizing factor in other diseases had not yet been established.

PREVENTION AND MODIFICATION; HOME CASES AND INSTITUTIONAL CASES

As noted by Eley⁵ and previously by Karelitz⁴ there is considerable difference in the actual administration of this immunologic agent, depending on whether measles is occurring in the private home or in institutions. Karelitz, Greenwald and Klein,⁷ after reviewing the work of McKhann and his associates,³ decided to employ immune globulin (human) in the treatment of intimate home exposures, feeling that this would give a more adequate test and more accurate evaluation of the product than was obtained with McKhann's institutional series. As previously

TABLE 1.—Results Obtained by Karelitz

Authors	Dosage	No.	Pro- tected	Modi- fied	Falled
Morales and Mandry: Bol. Asoc. med. de Puerto Rico 22 : 217 (Nov.) 1930	10 cc. of adult serum	138	40%	40%	20%
Karelitz and Schick: J. A. M. A. 104 : 991 (March 23) 1935	10 cc. of adult serum	70	42%	41%	17%
Karelitz: New York State J. Med. 35 : 876 (Sept. 1) 1935	33-20 cc. immune globulin calculated to correspond to 10 cc. of adult serum	74	55%	42%	20%

noted, after varying their dosage in accordance with their own standardization (given previously) they obtained results which were comparable to those obtained with 10 cc. of adult serum.

Laning and Horan¹¹ employed immune globulin in a series of ninety-three cases. No serious case of measles developed, and in the typical cases which occurred complications did not develop. There was a control series of forty-six cases in which there were twenty-six severe cases, in fifteen of which complications occurred and two of which were fatal. These authors did not encounter alarming reactions and believed that the preparation was comparable to convalescent serum. They pointed out that it had the advantage of always being available. These authors administered 2 cc. to seven patients and 10 cc. to twelve patients from one to four days after exposure. The seven patients had light attacks of measles and the disease was prevented in the twelve cases. They then administered 2 cc. in seventy-four cases in which it was difficult to determine the date of exposure and the optimum time for administering a modifying dose. Light cases of measles developed in sixty-eight and moderate cases of measles in the six others. There were no severe cases and no

10. Blackler, C. F.: Adult Immune Serum in Measles Control, *Canad. Pub. Health J.* **27**: 557 (Dec.) 1936.

11. Laning, G. M., and Horan, T. N.: Immune Globulin Used as Preventive and Modifier of Measles, *J. Michigan M. Soc.* **31**: 772 (Dec.) 1935.

complications among those who were given immune globulin. The results are indeed surprising, since the modifying agent was given in this series at various indefinite points between exposure and prodromal symptoms.

Gottlieb¹² published a preliminary report on the use of immune globulin in the prevention of German measles in a hospital. In sixteen cases, all subjects being members of the staff, he injected 4 cc. intramuscularly and in another forty-six similar cases he injected 0.2 cc. intradermally. German measles did not develop in any of these cases, whereas nine cases of German measles developed in the control series of eighteen untreated similar cases. He expressed the hope that his report would stimulate further experimentation in the field and concluded that immune globulin was a useful measure for the prevention of the spread of an epidemic of German measles in an institution.

Goldstein, Eisenoff and Blauner¹³ reported on the use of immune globulin in an institutional epidemic of measles. These workers did not attempt to immunize all the patients in the hospital at once but determined first that exposure had taken place in each ward and on each floor before instituting immunization of patients in that section of the hospital. Goldstein and his co-workers immunized forty-nine persons, thirty-two of whom developed measles, five severe and twenty-seven mild, and only five developed complications. None of the persons who developed measles died but it is evident from the authors' results that there was a reduction in the severity of the disease and in the complications resulting from measles.

Salazar de Souza,¹⁴ after referring to his original report¹⁵ on the use of placental blood, noted that the 1934 Lisbon epi-

fractions with the hope of finding a preparation equally successful but with fewer reactions. In all instances he found that refinement and concentration resulted in lowered potency, although all the preparations had some immunizing activity. Later he used the immune globulin orally in an attempt to avoid measles.

ORAL ADMINISTRATION

McKhann, Green, Eckles and Davies¹⁷ were able to render twenty-two children negative to the Dick test for periods up to eighteen days by the oral administration of from two to three times the amount of immune globulin (human) that is usually injected for immunization against measles. (Periods lasting eighteen days occurred only if the immunizing substance was served in iced alkaline carbonated water.) The preparation was always administered in cold water on an empty stomach. These results could not be obtained in adults, although the authors believed that the test suggested the effectiveness of the oral administration of this substance in the prevention and modification of measles. This was done in an attempt to avoid reactions seen with the injection of this material. In accordance with their expectations, no reactions occurred in the series of twenty-two patients given the substance orally. Table 2 indicates their study of the oral administration of immune globulin (human) for prevention and modification of measles. It is obvious that the results were not particularly good but also that it at least had the advantage of not producing any reactions.

It is obvious from the results in this small series of cases that the oral administration of this preparation is still in an early experimental stage.

AVAILABILITY

One of the principal advantages of the use of immune globulin (human) is that it is more available than the other agents which are used for the same purpose. This fact has been pointed out by many of the authors who have promoted and continued the study of its usefulness. Chu and Chou¹⁸ went one step further and prepared a dry form which they found convenient for the purpose of pooling and of storage without deterioration. They tested the product in a series of twenty-two cases by intramuscular injection with the following results: prevention, five cases; very mild measles, seven cases; mild measles, two cases; slightly modified measles, five cases, and unmodified measles, three cases.

SUMMARY

At the time of the previous consideration by the Council of immune globulin (human) the evidence was considered inadequate on which to give it further consideration. A study of the literature which has become available since that report was published indicates that the following points are of importance:

1. The use of the diphtheria antitoxin titer is entirely satisfactory as an adequate basis for determination of the measles immunizing potency of the preparations.

2. The degree of modification which is accomplished by the various immunizing preparations apparently determines whether or not a temporary or permanent immunity is conferred.

3. The reports seem to be about equally divided on the question of whether or not this immunizing agent is superior to convalescent serum.

4. It is as useful for the modification of measles in home cases as it is for prevention in institutional cases.

5. The reactions are not infrequent and not always mild following the use of this agent, and attempts to avoid them have included refinement and concentration as well as oral administration instead of injection of the immunizing agent.

6. The preparation has a greater availability than the other immunizing agents.

7. The advantages and disadvantages of immune globulin (human) as an immunizing agent in the prevention and modification of measles are at least equal to those of other preparations which have been used for a similar purpose.

17. McKhann, C. F.; Green, A. A.; Eckles, L. E., and Davies, J. A. V.: Immunologic Applications of Placental Extracts: Effectiveness by Oral Administration, *Ann. Int. Med.* 9: 388 (Oct.) 1935.
18. Chu, F. T., and Chou, C. Y.: Use of Dry Form of Placental Extract in Modification of Measles, *Chinese M. J.* 50: 297 (April) 1936.

TABLE 2.—Results Obtained by McKhann, Green, .
Eckles and Davies

		Protected	Modified	Failed
Given to prevent*.....	18	7	5	6
Given to modify†.....	66	15	32	19

* Early in incubation period.

† Late in incubation period.

demie had given him an additional opportunity to complete his research in this field. He at first had used formaldehyde in the preparation of his serum and blood, but he found that this attenuated the immunizing factors and substituted tyndallizations of from 52 to 54 degrees. He later added merthiolate 1:1,000, one part to three of the finished serum, and found that the immunizing factor was not attenuated. He continued, however, to use a single tyndallization at 54 degrees for one hour. Using from 4 to 5 cc. of the preparation derived in this manner, he obtained immunization in 80 per cent of his cases and using from 6 to 6.5 cc. in another series he obtained immunization in 100 per cent of the cases. He noted the failure reported by Accordini¹⁶ but felt that the results obtained by the latter, while negative, were more or less in accord with the fact that the injections were given from the fifth to the eighth day rather than before the fifth day after exposure.

REACTIONS

In one series of ninety-three cases¹¹ there were eighteen reactions, eight of which occurred from the administration of 10 cc. doses. Reactions were both local and general but subsided within twenty-four hours. There had been local reactions in 35 per cent, severe local reactions in 4 per cent and febrile reactions in 15 per cent, with temperatures of 101 F. in 2.5 per cent. Karelitz⁴ considered the reactions a distinct disadvantage. McKhann⁶ studied the immunizing property of globulin

12. Gottlieb, Julius: Placental Extract in the Control of German Measles: Preliminary Report, *Maine M. J.* 27:10 (Jan.) 1936.

13. Goldstein, Hyman; Eisenoff, Henry M., and Blauner, Samuel A.: Use of Immune Globulin in the Prophylaxis of Measles, *Am. J. Dis. Child.* 53:110 (Jan.) 1937.

14. Salazar de Souza, Jaime: Immunization Against Measles by Placental Blood, *Arch. de méd. d. enf.* 33: 282 (May) 1936.

15. Salazar de Souza, Jaime: Active Specific Transitory Immunization Against Measles by Use of Placental Blood, *Arch. de méd. d. enf.* 35: 633 (Nov.) 1932.

16. Accordini, G.: Morbillo ed immunizzazione (Results of Immunization with Placental Blood), *Clin. Pediat.* 15: 572 (July) 1933.

NEW AND NONOFFICIAL REMEDIES

THE FOLLOWING ADDITIONAL ARTICLES HAVE BEEN ACCEPTED AS CONFORMING TO THE RULES OF THE COUNCIL ON PHARMACY AND CHEMISTRY OF THE AMERICAN MEDICAL ASSOCIATION FOR ADMISSION TO NEW AND NONOFFICIAL REMEDIES. A COPY OF THE RULES ON WHICH THE COUNCIL BASES ITS ACTION WILL BE SENT ON APPLICATION.

PAUL NICHOLAS LEECH, Secretary.

IMMUNE GLOBULIN (HUMAN).—A preparation of globulins made from human placental blood and containing immune factor or factors against measles. The immunizing potency of the product is determined on the basis of the diphtheria antitoxin titer of the placental blood.

Actions and Uses.—Immune globulin (human) is useful in the prevention and modification of measles. It is equivalent in usefulness to convalescent serum but has the advantage of universal availability. It has the disadvantage of producing reactions not always mild. Most reactions, however, can be avoided by the administration of the proper dosage, which is necessarily modified in accordance with the stage of the incubation period or the prodromal stage of the disease. It is useful in the prevention of measles in institutional cases in larger doses than those given for modification. Prevention is, of course, less desirable than modification except where younger children ill with other diseases are apt to contract measles by exposure to a modified case. Otherwise it is more desirable to permit a child to have mild measles so that immunization occurs rather than to prevent the disease and leave the child nonimmune to subsequent attacks of the disease. Protection should not be attempted until definite exposure has taken place. Immune Globulin (Human) has also been used in the treatment of measles. Attempts to avoid reactions have led to refinement and concentration of the product and even to its oral administration, which cannot be advocated on the basis of the evidence which is available at present.

Dosage.—The amount of immune globulin (human) which should be injected in a given case depends on the following factors:

1. Whether modification or prevention is desired.
2. The age and general condition of the patient.
3. The intimacy of exposure, the stage of the disease and the virulence of the infection.

Careful consideration of the available literature is necessary to evaluate properly these factors and determine an entirely satisfactory dosage, and even then it is not always possible to be certain of not obtaining prevention when modification is desired and vice versa. The following doses are recommended merely as a general pattern and are subject to adjustment in accordance with the factors listed above: for prevention, 2 to 5 cc.; for modification, 2 to 10 cc.; for treatment (with caution), 5 to 10 cc.

E. R. Squibb & Sons, New York.

Immune Globulin (Human).—(Placiminium).—Human placentas from healthy mothers are extracted with 2 per cent sodium chloride solution for forty-eight hours at approximately 40 F. The soluble material is decanted, centrifuged and refined in a manner essentially that used in the concentration of antitoxins, ammonium sulfate being used as a precipitant. The final precipitate containing the antibody-bearing globulins is dialyzed to remove sulfates, centrifuged, filtered through a bacteriologic filter, tested for sterility and assayed on guinea pigs for its power to neutralize a measured dose of diphtheria toxin.

Marketed in packages of 2 cc. and 10 cc. vials, each sealed with a rubber diaphragm.

DIPHTHERIA TOXIN-ANTITOXIN MIXTURE

(See New and Nonofficial Remedies, 1938, p. 406).

The Gilliland Laboratories, Inc., Marietta, Pa.

Diphtheria Toxin-Antitoxin Mixture, 0.1 L+ (Goat).—Each cubic centimeter represents 0.1 L+ dose of diphtheria toxin neutralized with the required amount of diphtheria antitoxin obtained from the goat. Marketed in packages of three 1 cc. vials, and in packages of three 1 cc. syringes (one immunizing treatment); in packages of thirty 1 cc. vials (ten immunizing treatments); and in single vial packages containing, respectively, 10 cc., 20 cc., and 30 cc.

ANTI-PNEUMOCOCCIC SERUM, TYPE II (See New and Nonofficial Remedies, 1938, p. 399).

Parke, Davis & Company, Detroit.

Antipneumococcic Serum (Felton) Type II, Refined and Concentrated.—An anisum containing predominantly antibodies of type II pneumococcus (Diplococcus pneumoniae) prepared by immunizing horses with killed cultures of highly virulent Diplococcus pneumoniae isolated from lobar pneumonia. The product is refined and concentrated by the method of Dr. L. D. Felton (*J. Infect. Dis.* 43:543 [Dec.] 1928) and contains antibacterial properties against type II Diplococcus pneumoniae. The potency of the product is expressed in terms of the unit described by Dr. Felton, one unit being that amount of serum which, when injected simultaneously with a given test dose of culture, will protect for ninety-six hours at least 60 per cent of the test mice. It is also tested by the precipitation test designed by Dr. Felton. The finished product contains

some type I pneumococcus antibodies. It is marketed in two packages of one syringe, one containing 10,000 and the other 20,000 Felton units of type II Diplococcus pneumoniae; each package contains also a vial of normal horse serum (1:10 dilution) for reaction test.

THIAMIN CHLORIDE (See THE JOURNAL, July 16, 1938, p. 253, and the Supplement to N. N. R., 1938, p. 17).

Thiamin Chloride-Squibb.—A brand of thiamin chloride-N. N. R.

Distributed by E. R. Squibb & Sons, New York.
Ampule Solution Thiamin Chloride-Squibb, 1 cc.
Tablets Thiamin Chloride-Squibb, 1 mg.
Tablets Thiamin Chloride-Squibb, 5 mg.

EPHEDRINE SULFATE (See New and Nonofficial Remedies, 1938, p. 228).

Ephedrine Sulfate-Upjohn.—A brand of ephedrine-sulfate-U. S. P.

Capsules Ephedrine Sulfate-Upjohn, 3/4 grain (0.025 Gm.).
Capsules Ephedrine Sulfate-Upjohn, 3/4 grain (0.05 Gm.).
Ampoules Ephedrine Sulfate-Upjohn, 3/4 grain (0.05 Gm.).
Manufactured by The Upjohn Co., Kalamazoo, Mich. No U. S. patent or trade mark.

COUNCILS' COMMITTEE ON CONTRACEPTIVES

THE FOLLOWING REPORT WAS PREPARED UNDER THE AUSPICES OF THE COUNCILS' COMMITTEE ON CONTRACEPTIVES AND PUBLICATION HAS BEEN AUTHORIZED.

PAUL NICHOLAS LEECH, Secretary,
Council on Pharmacy and Chemistry.

HOWARD A. CARTER, Secretary,
Council on Physical Therapy.

REPORT ON THE USE OF ROENTGEN RAYS FOR CONTRACEPTION

In 1932 Harris¹ and in 1936 Mayer, Harris and Wimpfheimer² published articles dealing with the use of roentgen rays to produce therapeutic abortion. Their results were satisfactory and, in their opinion, superior to surgical procedures in pregnancies of less than fourteen weeks' duration. This method they advocated as particularly desirable in cases in which surgery is hazardous or contraindicated for medical reasons. Following this treatment there is a period of amenorrhea for about two years in women under 35 years of age. In women over 35 the amenorrhea may be permanent.

At the organization meeting of the Councils' Committee on Contraceptives, it was suggested that roentgen rays had been used to cause sterility in women or to interrupt pregnancy for nonmedical reasons. The impression was given that this procedure may be more generally practiced than is believed. Dr. A. U. Desjardins, in an effort to determine how extensively roentgen rays are being used for these purposes, wrote to twelve radiologists throughout the country. In all but one instance the replies from these men stated that they were not aware of such a practice, certainly on the part of reputable members of the profession, and were doubtful whether this technic was being employed to any appreciable extent by less scrupulous practitioners. That this practice has been conducted by a few physicians has apparently come to the attention of a prominent radiologist in an eastern city, but he adds that there has been no legal issue, to his knowledge.

If roentgen rays are being used to induce abortion or to produce sterility it seems highly improbable that it is a very common practice, as it has not come to the attention of radiologists throughout the country. Certainly reputable radiologists are not engaged in this practice and, if men of lesser ethical principles are employing this method, they are doing so very unobtrusively. In spite of the results reported by the workers mentioned in the use of roentgen rays for therapeutic abortion, it is the opinion of radiologists and other members of the medical profession that this method is decidedly dangerous and that its use should be deprecated. It is needless to say that the use of roentgen rays to produce abortion in cases in which emptying of the uterus is not required for therapeutic reasons is contrary to all the ethical principles of medical practice.

1. Harris, William: *Am. J. Roentgenol.* 27:415 (March) 1932.
2. Mayer, M. D.; Harris, William, and Wimpfheimer, Seymour: *Am. J. Obst. & Gynec.* 32:945 (Dec.) 1936.

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

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SATURDAY, NOVEMBER 5, 1938

ISOLATION FROM HUMAN BEINGS OF EQUINE ENCEPHALOMYELITIS VIRUS

In this issue of THE JOURNAL are two papers (pages 1734 and 1735) reporting in two widely separated areas in the United States cases of human encephalitis, the causal relation of which to epidemic equine encephalomyelitis seems to have been proved. One of the outbreaks apparently was due to the western strain and the other outbreak due to the eastern strain of equine encephalomyelitis.

Isolation of eastern equine encephalomyelitis virus from the brains of children who died from encephalitis and proof that the virus thus isolated is infectious on intranasal instillation into mice are recent notable contributions to epidemiologic knowledge.¹ This is apparently the first horse virus definitely implicated in a human disease.

During August and September an outbreak of the eastern type of equine encephalomyelitis occurred in southeastern Massachusetts, accompanied by several fatal cases of encephalitis among children. Fothergill and his colleagues² reported the isolation of the horse virus from the brain of one of these patients. Brain tissues from seven other patients were placed in sterile glycerin by Pope and Feenster of the Massachusetts State Department of Health and sent to Webster and Wright³ of the Rockefeller Institute for detailed microbic analysis. The New York consultants made a 10 per cent suspension of these tissues in hormone broth and injected 0.03 cc. doses of the resulting supernatant fluid intracerebrally into 3 weeks old Swiss mice. Forty-eight hours later mice injected with four of the seven human brain samples showed ruffled fur and lethargy, alternating with slight convulsive twitchings. The mice soon became prostrate, showed severer and more frequent convulsive movements, and died by the seventy-second hour. Cultures from the brains and

organs of these mice were bacteriologically sterile. The brains of certain of these mice were emulsified and injected intracerebrally into second generation mice. Mice thus injected became ill within forty-eight hours and died within seventy-two hours. Third and fourth generation mouse brains were emulsified and filtered through a Seitz pad. Mice injected with the resulting filtrates developed typical symptoms and succumbed by the third day. This successful filtration proved that the infectious agent is a virus of relatively small dimension.

The virus was found to be highly infectious for mice by nasal instillation. Third generation mouse passage virus was fatal to monkeys and guinea pigs when injected intracerebrally in large doses. By the forty-eighth hour the animals appeared dazed, showed muscle weakness and then became prostrate, death usually occurring between the seventy-second and the ninety-sixth hour. Blood and spinal fluid taken at the forty-eighth hour stage were positive for the virus (mouse test). Brains removed just before or soon after death were also infectious. Rabbits were also susceptible to massive intracerebral doses of the virus and usually succumbed within seventy-two hours. Their brain tissues gave positive mouse tests for the infectious agent. Guinea pigs given the virus in the pad usually developed a fatal encephalitis after a latent period of about five days. The relative susceptibilities of the five animal species are characteristic of the eastern horse encephalomyelitis virus. These susceptibilities differ from those of other known viruses which cause infection of the central nervous system in man.

The presumptive identity with the horse virus was confirmed by specific neutralization tests. Of each of the four positive brain emulsions 0.3 cc. was mixed with an equal volume of hyperimmune antiequine-encephalomyelitis rabbit serum (eastern strain). Serial dilutions of the resulting mixtures were injected intracerebrally into mice, with duplicate intraperitoneal injection by the Olitsky technic.⁴ The immune serum showed protection effects against from 1,000 to 1,000,000 minimal lethal doses of the brain suspensions. Control tests with normal rabbit serum showed no protection, nor would a specific antiserum against the western strain of horse encephalomyelitis neutralize the infectious agent. This completed the proof of the identity of the human virus with the eastern horse virus.

Now also for the first time neutralization of the western virus of equine encephalitis by human serum has been found.⁵ A study of the possibilities of vaccine therapy is now in progress among veterinarians. The conceivable role of field or domestic mice as possible carriers is also under investigation.

1. Wesselhoeft, Conrad; Smith, E. C., and Branch, C. F.: Human Encephalitis, this issue, p. 1735.

2. Fothergill, L. D.; Dingle, J. H.; Farber, Sidney, and Connerley, M. L.: New England J. Med. 219: 411 (Sept. 22) 1938.

3. Webster, L. T., and Wright, F. H.: Science 88: 308 (Sept. 30) 1938.

4. Olitsky, P. K., and Harford, C. G.: J. Exper. Med. 68: 173 (Aug.) 1938.

5. Eklund, C. M., and Blumstein, Alex.: The Relation of Human Encephalitis to Encephalitis in Horses, this issue, p. 1734.

RECENT DEVELOPMENTS IN THE TREATMENT OF UNDULANT FEVER

The increased recognition and incidence of undulant fever has fortunately been associated with new and improved methods of treating this disease, in both its acute and its chronic form. Vaccination has been employed for about ten years, in many instances with apparent success. Huddleson and Johnson¹ have used a liver broth filtrate of the *Brucella* organism for intramuscular injection. This preparation is known as brucellin; the intramuscular injection of this filtrate has usually resulted in a local reaction and a rise in temperature. If precautions are taken to determine the sensitiveness of the patient before administration, these authors believe that it can be used without dangerous consequences. Foshay and his associates² have employed detoxified bacterial antigens in the preparation of an antiserum for the treatment of undulant fever. Goats were used at first in the preparation of this antiserum but more recently horse serum has proved equally satisfactory. Flippin³ has recently reported encouraging results in the treatment of five cases of undulant fever with a sterile polyvalent antimelitensis serum of bovine origin. Convalescent serum, transfusion with whole blood and vaccines prepared in still other ways⁴ have also been reported as sometimes successful in the treatment of this disease. While sufficient evidence has not yet become available to determine which of these methods of therapy is the more effective, they offer, nevertheless, a hopeful and, at least in some instances, an apparently effective means of therapy.

During the past year favorable reports of the treatment of undulant fever with sulfanilamide or its compounds have rapidly accumulated. Among the reports of successful treatment with sulfanilamide or its derivatives are those by Toone and Jenkins,⁵ Manson-Bahr,⁶ Richardson⁷ and Stern and Blake.⁸ From the information available it seems likely that sulfanilamide in rather large doses is necessary but that at least in some resistant cases the results are comparable, if not superior, to any other form of treatment of undulant fever thus far proposed.

Finally, successful results have been claimed for other recently described forms of therapy in undulant fever. Among them are treatment by physically induced

hyperpyrexia⁹ and the intravenous administration of neoarsphenamine.¹⁰ Although a decision as to the value of any method of treatment in undulant fever is difficult because of the alternation of febrile periods and afebrile pauses, the available methods of therapy are such as to allow the disease to be met with a much more powerful therapeutic armamentarium than existed a few years ago.

PROSTITUTING THE INITIATIVE!

In several states by constitutional amendment the people have the right to vote directly on legislation which they themselves initiate or on measures already passed by the legislature. By this means the laws of the state may be made more clearly to reflect the will of a majority of the voters. The initiative procedure, however beneficial its attributes may be theoretically, has unfortunately been utilized by small groups to foster schemes for selfish ends. On November 8 the people of three states will vote on measures initiated by such groups.

In California a measure initiated by a small group of emotionalists seeks to cripple scientific research in the state by making it difficult if not impossible to procure animals for experimental purposes. In Oklahoma an initiative measure proposes, among other things, to permit hospitals legally to enter into contracts for medical services, if the hospital is organized "on a mutual and cooperative nonprofit plan in connection with some recognized farm or labor union or church or charitable organization." In Colorado, initiative amendment No. 2 proposes by constitutional amendment to guarantee to every person in the state the exclusive right to choose his own state license system of healing and physician for state-required examinations or for therapeutic services in connection with state compensation or other insurance benefits and to open the doors of all tax-supported or partially tax-supported corrective, therapeutic or eleemosynary or other public institutions in the state to the cultists. The Colorado amendment, if adopted, will repeal the basic science act enacted by the legislature in 1937, will deprive the legislature of any future right to exercise its police power in protecting the people from the ministrations of incompetent healers and will devolve on any profession recognized by the state the "exclusive right to examine, license and regulate the practice of its own members through its own legally constituted power or authority."

It seems inconceivable that these measures will receive the approval of the voters in these three states. The tragedy lies in the fact that a procedure conceived in the public interest may be invoked and utilized for purposes inimical to that public interest.

1. Huddleson, J. F., and Johnson, H. W.: "Brucellin" a Possible Specific for Undulant Fever in Man, *Am. J. Trop. Med.* 13:485 (Sept.) 1933.

2. Wherry, W. B.; O'Neil, A. E., and Foshay, Lee: Brucellosis in Man: Treatment with a New Antiserum, *Am. J. Trop. Med.* 15:415 (July) 1935.

3. Flippin, H. F.: Treatment of Undulant Fever: A Report of Five Cases Treated with a Specific Polyvalent Serum, *Ann. Int. Med.* 12:232 (Aug.) 1938.

4. Carr, J. G.: The Symptoms, Diagnosis and Treatment of Undulant Fever, *Illinois M. J.* 73:521 (June) 1938.

5. Toone, E. C., and Jenkins, A. M.: Undulant Fever (Brucellosis) Treated with Sulfanilamide, *Arch. M. J.* 31:478 (May) 1938.

6. Manson-Bahr, C.: Action of Sulfanilamide on *Brucella Abortus*, *Am. J. Trop. Med.* 140:740 (June) 1938.

7. Richardson, L. A.: Infection with *Brucella Abortus* Treated with Protonsil, *Lancet* 1:495 (Feb. 26) 1938.

8. Stern, R. L., and Blake, K. W.: Undulant Fever: Its Treatment with Sulfanilamide, *J. A. M. A.* 110:1550 (May 7) 1938.

9. Prickman, L. E.; Bennett, R. L., and Krusen, F. H.: Treatment of Brucellosis by Physically Induced Hyperpyrexia, *Proc. Staff Meet., Mayo Clin.* 13:321 (May 25) 1938.

10. Wainwright, C. W.: Melitensis Infection: Treatment with Neoarsphenamine, *South. M. J.* 30:600 (June) 1937.

AMERICAN PUBLIC HEALTH ASSOCIATION MEETING

Elsewhere in this issue (page 1775) appears a brief summary of the discussions relating to medical care at the recent meeting of the American Public Health Association in Kansas City, together with resolutions adopted by the association. Apparently the American Public Health Association failed to place its endorsement on the expressed desire of the president-elect, Dr. Abel Wolman, a doctor of engineering, for the endorsement of the National Health Program in toto as presented by the Technical Committee to the National Health Conference held at Washington in July. Instead it endorsed the proposals of the National Health Conference relating to increased public health services, improvement of hospitalization facilities, care of the medically indigent and compensation for wage losses due to sickness. With respect to the development of health insurance specifically, the association remained silent. It did, however, endorse the statement of the Technical Committee that wide latitude should be given to the development of state plans for carrying out any changes proposed in the delivery of medical service.

The discussion of this issue apparently developed a sharp cleavage in the membership of the American Public Health Association. The lay members of the association, including engineers and sanitarians, were disposed to follow the government's proposals as outlined in the National Health Conference without modification. The medical members of the association, however, including leaders among health officers, executives of volunteer agencies and teachers of public health, were opposed to the endorsement of health insurance proposals made at the National Health Conference. The counsel of the latter group prevailed and the American Public Health Association, therefore, stands officially on virtually the same platform as the American Medical Association. So also does the Conference of State and Provincial Health Authorities of North America. The appointment of a committee of the American Public Health Association to confer with the President's Technical Committee also parallels the action of the American Medical Association.

With the main body of physicians and the main bodies of public health workers committed essentially to the same set of principles and in accord with the government on most of these principles, the best service to the public health may now be rendered by cooperation on those points on which agreement has been reached. Physicians are too important to the public health program and public health workers too important to the physician for either group to permit extremists to drive wedges between them. Efforts to alienate the people from their physicians reflect little credit on the integrity or the judgment of those who

indulge in such tactics. The physician stands committed today, as always, to progress in public health, in hospitalization, in medical care for the needy and in defense of the quality of medical care.

Current Comment

THE COUNCILS' COMMITTEE ON CONTRACEPTIVES

The House of Delegates at its meeting in Atlantic City in 1937 delegated to the Council on Pharmacy and Chemistry and to the Council on Physical Therapy the problem of the investigation of materials, devices and methods recommended or employed for the prevention of conception with a view to determining their physiologic, chemical and biologic properties and effects. The two councils appointed representatives and last spring a Councils' Committee on Contraceptives was organized. The committee is charged simply with studies affecting problems of therapeutic contraception and problems of sterility as well. The first report, which appears on page 1767 in this issue of *THE JOURNAL*, concerns the misuse of roentgen rays to induce abortion or to produce sterility.

INTRANASAL MEDICATION

Last year *THE JOURNAL*¹ called attention to the danger of "lipoid pneumonia" following the intranasal administration of oily preparations. Recently Walsh and Cannon² reported that oil, when given in large total amounts and over a long period in this manner to normal rabbits free from upper respiratory infections, seemed to initiate lesions in the lungs which could be demonstrated in roentgenograms. Edema, desquamative alveolitis and focal lipoid pneumonia were produced. As pointed out by these investigators, nasal oils when used clinically or employed because of rhinitis or upper respiratory disease, in passing through infected areas are likely to carry live organisms to the lungs. The combined effect of these factors, therefore, is serious. They instilled medicated oil into a normal rabbit, followed twenty-four hours later by a suspension of live micro-organisms cultured from a rabbit with snuffles; granulomatous lesions were discovered throughout both lungs twenty days after the treatment. These granulomatous lesions contained oil. Intranasal administration of watery solutions of such commonly used medicaments as neosilvol, mild protein silver, tannic acid, zinc sulfate and sodium sulfate, they found, resulted in pulmonary lesions including edema, necrosis and desquamation of macrophages. Such lesions were particularly frequent when antiseptics were given intranasally to rabbits with snuffles or when given mixed with living micro-organisms. The Chicago investigators found that isotonic saline solutions containing such vasoconstrictors as ephedrine and neosynephrin did not cause pulmonary

1. Lipoid Pneumonia and Oil in the Lungs, *Current Comment*, J. A. M. A. 109:1367 (Oct. 23) 1937.

2. Walsh, T. E., and Cannon, P. R.: The Problem of Intranasal Medication, *Ann. Otol., Rhin. & Laryng.* 47:579 (Sept.) 1938.

damage after intranasal instillation in normal rabbits. This work, the reports of others, and the additional observations of the same workers³ point to the potential dangers of intranasal medication and to the tentative conclusion that the only completely safe intranasal medicaments are weak saline solutions of appropriate vasoconstrictors. The use of nose drops containing antiseptics, astringents or oily solutions may be, therefore, of doubtful advisability because of manifest irritating effects on the lungs.

Association News

HEARINGS BEFORE THE GRAND JURY IN WASHINGTON

Subsequent to the hearing of the witnesses mentioned in THE JOURNAL last week, the witnesses now include Mr. R. R. Zimmerman, personnel director of the Federal Home Loan Bank Board. Newspapers state that, before Mr. Zimmerman testified, the Grand Jury convened several hours privately with the assistants to the Attorney General who are presenting the government's evidence. Another witness was Mr. William F. Penniman, deputy governor of the Home Loan Bank System and first president of the Group Health Association, Inc. Another witness was Dr. Mario Scandiffo, a member of the staff of the Group Health Association, Inc., and Miss Mary Frances Stuart, laboratory technician of the Group Health Association, Inc. Other witnesses were Dr. Louis R. Marshall of the Veterans Administration Hospital at Batavia, N. Y., and Dr. J. Keith Cromer of Washington, D. C., an obstetrician.

STATE HEALTH AUTHORITIES SUPPORT AMERICAN MEDICAL ASSOCIATION

The Conference of State and Provincial Health Authorities of North America, in executive session at Kansas City, Mo., October 26, passed the following resolution:

Resolved, By the State and Provincial Health Authorities of North America, assembled in special session this twenty-sixth day of October, nineteen thirty-eight, that we hereby express our appreciation and commendation to the House of Delegates of the American Medical Association for their considered action this past September concerning the recommendations laid before our profession at the National Health Conference at Washington, D. C., this past July.

F. J. UNDERWOOD, President.
A. J. CHESLEY, Secretary.

RADIO BROADCASTS

The fourth series of programs broadcast in dramatic form portraying fictitious but typical incidents of significance in relation to health by the American Medical Association and the National Broadcasting Company, entitled "Your Health," began Wednesday October 19 and will run consecutively for thirty-six weeks. The program is broadcast over the Blue network of the National Broadcasting Company each Wednesday at 2 p. m. eastern standard time (1 p. m. central standard time, 12 noon mountain time, 11 a. m. Pacific time).¹

These programs are broadcast on what is known in radio as a sustaining basis; that is, the time is furnished gratis by the radio network and local stations and no revenue is derived from the programs. Therefore, local stations may or may not take the program, at their discretion, except those stations which are owned and operated by the National Broadcasting Company.

The programs to be broadcast in the first group, together with their dates and their topics, are as follows:

- Nov. 9. Healthier Boys and Girls.
- Nov. 16. Healthful Play.
- Nov. 23. Weather and Wearing Apparel.

3. Cannon, P. R., and Walsh, T. E.: Lipoid Pneumonia and Some Potential Dangers of Intranasal Medication. Internat. Clin. 3: 109, 1938.
1. Owing to program conflicts, there will be no Chicago broadcast of the network program. Instead, a recording of the program will be broadcast over Station WENR at 8 p. m. each Wednesday. This recording will be an identical rebroadcast of the network program broadcast earlier the same day.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

CALIFORNIA

Exhibit—The March of Life.—A sixteen unit display entitled "The March of Life" will make up the exhibit of the University of California Medical School at the Golden Gate International Exposition in 1939. The presentation will show what medicine and surgery have accomplished since the time of Hippocrates and, in addition, demonstrate the services rendered by the university's medical center to its own students.

Annual San Joaquin Graduate Course.—The fourth annual graduate study course of the San Joaquin County Medical Society began in Stockton September 22 and will continue each week until November 17. Participating in the course are the following, among others:

- Dr. William Dock, San Francisco, Its Interpretation and Its Application in . . .
- Dr. Hans Lissner, San Francisco, . . . as Seen in Hyperthyroidism, Myxedema, . . . Addison's Disease, Cushing's Disease.
- Dr. James W. Morgan, San Francisco, Proctology.
- Dr. Elliot P. Smart, Murphys, Thoracoplastic Operations.
- Dr. William J. Kerr, San Francisco, Clinical Presentation of Medical Cases.

Symposium on Heart Disease.—The San Francisco Heart Committee of the San Francisco County Medical Society will hold its ninth annual graduate symposium on heart disease November 15-17. Sessions will be held at the San Francisco, Stanford University and University of California hospitals and Laguna Honda Home. The morning meetings will be devoted to study groups limited to five or ten physicians, covering demonstration of patients presenting problems in heart disease, evaluation of specific diagnostic procedures and therapy, differential diagnosis and treatment. General sessions will be held in the afternoons and evenings; on Tuesday afternoon the diagnosis and treatment of heart irregularities will be discussed; Wednesday, problems in degenerative heart disease, and Thursday, therapy of heart failure. A public meeting will be held Wednesday evening.

FLORIDA

District Meeting.—The Southwest Medical District Society held its second annual meeting at the Dixie Grande Hotel, Bradenton, September 29, under the presidency of Dr. John W. Alsobrook, Plant City. Dr. John F. Mason, Bradenton, president, Manatee County Medical Society, gave the address of welcome. Other speakers, in addition to officers of the state medical society, included:

- Dr. Whitman C. McConnell, St. Petersburg, The Insured Neurotic.
- Drs. Jere W. Annis and John W. Vaughn, Lakeland, Myocardial Infarction: Electrocardiographic Changes and Necropsy Findings.
- Dr. Leldon W. Martin, Sebring, Meckel's Diverticulum.
- Dr. Nathan L. Marcus, Tampa, Case of Agranulocytosis with Review of Literature.

ILLINOIS

Society News.—At a meeting of the Tri-County Medical Society in Galesburg October 25 Dr. Warren H. Cole, Chicago, spoke on hyperthyroidism. —The Stephenson County Medical Society was addressed October 27 by Drs. Joseph K. Calvin and Abraham F. Lash, Chicago, on nephritis and puerperal sepsis, respectively. —Dr. Paul H. Harmon, Chicago, addressed the Woodford County Medical Society September 19 on "Diagnosis and Treatment of Suppurative Arthritis of the Hip with Special Reference to Pathologic Dislocation." —The third annual meeting of the Physicians' Association, state department of public welfare, was held in the rooms of the Kankakee County Medical Society, Kankakee, October 12. Dr. Abraham A. Low, assistant state alienist, discussed the newly organized association of former patients of the Psychiatric Institute of the Research and Educational Hospitals, University of Illinois, Chicago, and its implications for the entire group of mental patients, and Dr. Louis Belinson, Elgin, a comparative survey of antisyphilitic treatment in the state hospitals. —The Sangamon County Medical Society was addressed in Springfield October 6, among others, by Drs. Emmet F. Pearson and Darrell H. Trumpe on "Anatomy and Physiology of Chronic Bronchitis and Bronchial Asthma" and "Diagnosis and Management of Minimal Pulmonary Tuberculosis" respectively.

Dr. de Tarnowsky to Give Armistice Day Lecture.—Dr. George de Tarnowsky will deliver the Armistice Day lecture sponsored by the faculty and alumni of the University of Illinois College of Medicine Friday morning November 11 in room 423 of the medical school. His paper will be entitled "Twenty Years Later," in which he will review the work done by the medical, dental and nursing corps during the World War. Dr. De Tarnowsky is professor of surgery at the college of medicine.

Dr. Hektoen to Give Pasteur Lecture.—Dr. Ludvig Hektoen, executive director of the National Advisory Cancer Council, Washington, D. C., and director of the John McCormick Institute for Infectious Diseases, Chicago, will deliver the fifteenth Pasteur Lecture at a public meeting in the auditorium of the Museum of Science and Industry, Jackson Park, November 22. The lecture will be under the auspices of the Institute of Medicine of Chicago and the Cancer Research Institute of the Chicago Woman's Club. The subject will be "Progress in the Knowledge and Control of Cancer." Through the courtesy of the Museum of Science and Industry, the medical exhibits will be open specially for the meeting. The first Pasteur Lecture was given in 1920 and subsequently each year until 1931. Resumed in 1935, the lectures have been given annually since then. They are designed for laymen.

INDIANA

State Medical Election.—Dr. Karl R. Ruddell, Indianapolis, was chosen president-elect of the Indiana State Medical Association at its annual meeting in Indianapolis October 6 and Dr. Edmund M. Van Buskirk, Fort Wayne, was installed as president. Fort Wayne was designated the place for the meeting in 1939. The association went on record as approving plans for group hospitalization and voluntary sickness indemnity insurance provided they are controlled by physicians.

IOWA

Society News.—The Linn County Medical Society will be addressed November 11 by Dr. Roger Anderson, Seattle, Wash., on "Ambulatory Method of Treating Fractures of the Shaft of the Femur" and "Anatomic Method of Treating Fractures of the Leg." Dr. John P. Peters, New Haven, will discuss nephritis and medical economics before the society December 15.

Interprofessional Meeting.—The first annual public health program of the Iowa Interprofessional Association was held in connection with the annual meeting of the Iowa State Association of Registered Nurses in Waterloo October 12 with Dr. Ransom D. Bernard, Clarion, president of the interprofessional association, presiding. The following program was offered:

Harold V. Gaskill, Ph.D., assistant to the dean of industrial science, Iowa State College, Ames, Mutual Interests of the Professions in the Basic Sciences.
Dr. Clifford E. Waller, assistant surgeon general, U. S. Public Health Service, Washington, D. C., A National Health Program—A Review of the Program Recommended by President Roosevelt's Interdepartmental Committee to Coordinate Health and Welfare Activities.
Rev. Maurice Griffin, Cleveland, member, board of directors, American Hospital Association, National Health Conference and the Present Hospitals.

The Iowa Interprofessional Association is supported by the five professional state societies of medicine, dentistry, nursing, pharmacy and veterinary medicine.

MAINE

Society News.—The Kennebec County Medical Association was addressed at its first fall meeting in Waterville September 15 by Drs. John G. Towne on "Tuberculosis of the Bone"; Harvey J. Bourassa, "Ruptured Appendix"; Charles E. Towne, "Stricture of Urethra"; Ovide F. Pomerleau and Moses F. Lubell, "Three Cases of Cancer of the Cervix Treated with Radiation"; Theodore E. Hardy, "Chronic Glomerular Nephritis," and Edwin R. Irgens, "Nasal Plastics."

Graduate Education.—A program of graduate education was adopted at a meeting in Bangor October 2 of the editorial board of the *Maine Medical Journal*, the county secretaries, the president and the president-elect of the Maine Medical Association. One method will be the extramural or out of state education in which the physician will study in the larger medical centers through the help of the Commonwealth Fund and the Bingham Associates, while the second will be made available to physicians intramurally or within their own state by the importation of trained teachers who will visit the county medical societies at regular intervals.

MINNESOTA

Society News.—A symposium on sulfanilamide was presented before the Minnesota Pathological Society in Minneapolis October 18 by Drs. Raymond N. Bieter and Wesley W. Spink. Dr. Justus Ohage Jr. read a paper entitled "Primary Carcinoma of the Pancreas" before the Minnesota Academy of Medicine in St. Paul October 12. The Scott-Carver Medical Society was addressed at Montgomery October 11 by Drs. George D. Eitel and Ernest L. Meland, both of Minneapolis, on "Traumatic Surgical Emergencies" and "Urologic Emergencies." The Hennepin County Medical Society, Minneapolis, will be addressed November 7 by Dr. John L. McKelvey on "Gynecologic Malignant Tumors and Their Therapy." Drs. Edward T. Evans and Carl W. Laymon spoke November 2 on "Fractures in Children" and "Skin Disorders in Childhood" respectively.

MISSISSIPPI

Gift to Medical School Library.—The library of the late Dr. John A. K. Birchett, Vicksburg, consisting of more than 500 medical books and about 400 medical journals, was donated to the library of the University of Mississippi School of Medicine recently by his son, Dr. John A. K. Birchett Jr., an alumnus of the school.

Changes in Health Officers.—Dr. John W. Duggar, Jr., associated with the state department of health, has been appointed in charge of the Marshall County health department succeeding Dr. Vernon B. Harrison, Holly Springs, who has been granted a year's leave of absence to serve as assistant professor of bacteriology and preventive medicine at the University of Mississippi School of Medicine, it is reported.

NEVADA

Convention Advocates Health Program Under Existing Agencies.—The Nevada State Democratic Convention, held in Elko September 27, adopted the following resolution: We favor a public health program which does not interfere with the personal relations between physician and patient and that is administered through state agencies.

Committee on Industrial Health.—The president of the Nevada State Medical Association has appointed the following committee on industrial health: Drs. Ralph A. Bowdler, East Ely, chairman; Robert R. Craig, Tonopah, and Ontie Hovenden, McGill.

NEW YORK

Plans for Pneumonia Control.—Dr. Alexander D. Langmuir, medical consultant of the bureau of pneumonia control of the state department of health, Albany, conducted a series of conferences on pneumonia control in twelve Buffalo hospitals during the week October 10-15 under the auspices of the Medical Society of the County of Erie. Dr. Langmuir also conferred with members of the society who will address lay groups during the winter and gave a talk to nurses at the Buffalo General Hospital.

Society News.—Dr. Charles Sidney Burwell, Boston, addressed the Medical Society of the County of Albany, October 26, on "Diagnosis and Treatment of Constrictive Pericarditis." The Medical Society of the County of Nassau held its second annual members' night September 27; the speakers were Drs. William P. Bartels, Hempstead, on "Surgical Treatment of Acute Subdeltoid Bursitis"; Joseph Millett, Hempstead, "Diabetic Gangrene of the Face," and Carl J. Welge, Roosevelt, "Removal of Foci of Infection in Arthritis."

New York City

Legacy to Presbyterian Hospital.—A cash bequest of \$150,000 was left to Presbyterian Hospital in the will of Miss Susan D. Griffith, Saratoga Springs, N. Y., who died September 26. The residuary estate, the value of which was not declared, was also left to the hospital and the institution will receive in addition the principal of several trusts on their termination. The trusts will amount to about \$150,000.

New Superintendent of New York Hospital.—Dr. George Whiting Wheeler, assistant professor of applied bacteriology, Cornell University Medical College, and clinical bacteriologist at New York Hospital, has been appointed superintendent of the hospital to succeed Dr. Roger R. Hannon, who resigned October 1. Dr. Wheeler has been associated with the college and the hospital since his graduation from Cornell in 1907.

New Painting of William Beaumont.—Mr. Dean Cornwell held a private showing at the Waldorf-Astoria October 14 of a painting he recently finished entitled "Beaumont and St. Martin." This is said to be the first attempt by any artist

to reconstruct pictorially the setting and story of Dr. William Beaumont's epoch-making experiments on Alexis St. Martin at Forts Mackinac and Niagara, 1825 to 1835.

Lay Cornerstone for New College Building.—The ceremony of laying the cornerstone for a new \$1,500,000 building for the New York Medical College and Flower Hospital was held October 20. The date was the fiftieth anniversary of the laying of the cornerstone for the old college building and hospital at York Avenue and Sixty-Fourth Street. The new college will be at One Hundred and Fifth Street and Fifth Avenue. Mayor La Guardia placed the stone, in which were sealed a box from the old cornerstone containing photographs, coins and newspapers of fifty years ago with newspapers of October 20 and other clippings concerning the hospital's history. Besides Mayor La Guardia, speakers included Drs. George W. Crile, Cleveland; John L. Rice, commissioner of health, and Sigismund S. Goldwater, commissioner of hospitals.

Academy Lectures for the Public.—The fourth series of lectures to the public presented by the New York Academy of Medicine will begin November 10 with an address by Dr. Cecil K. Drinker, Boston, entitled "Not So Long Ago." The series will include:

- Dr. Karl A. Menninger, Topeka, Kan., *The Cinderella of Medicine*, December 8.
- Dr. Walter C. Alvarez, Rochester, Minn., *Emergence of Modern Medicine from Ancient Folkways*, Jan. 12, 1939.
- Dr. Roy Graham Hoskins, Boston, *The Story of Mental Diseases*, February 9.
- Dr. Charles Gordon Heyd, New York, *The Romance of Modern Surgery*, March 9.
- Dr. Sanford V. Larkey, Baltimore, *Health in Elizabethan England*, April 13.
- Dr. Livingston Farrand, Brewster, N. Y., *Primitive Man and Medicine*, May 11.

NORTH CAROLINA

Committee on Industrial Health.—Dr. Herman F. Easom, Raleigh, has been appointed chairman of a newly created committee on industrial health of the Medical Society of the State of North Carolina. Drs. Marion T. Plyler Jr., Nashville, and Gibbons W. Murphy, Asheville, will serve as members.

OHIO

Commissioner of Mental Diseases Appointed.—Dr. Jesse F. Bateman, superintendent of the Columbus State Hospital, has been appointed commissioner of a newly created division of mental diseases in the state welfare department. An advisory council for the division was also appointed by the governor as follows: Drs. Ora O. Fordyce, Toledo, and Louis J. Karnosh, Cleveland; Judge Dean May, Akron, and Judge Clifford M. Woodside, Youngstown.

PENNSYLVANIA

Cancer Meeting.—A program on cancer was presented at Beaver Falls October 13 under the auspices of the commission on cancer of the Medical Society of the State of Pennsylvania. In the afternoon Drs. Stanley P. Reimann, Philadelphia, and Thomas E. Jones, Cleveland, addressed physicians on "Necessity of Nonspecific Treatment of the Patient" and "Carcinoma of the Colon and Rectum" respectively. In the evening a public meeting was held with Dr. Samuel J. Waterworth, Clearfield, chairman of the cancer commission, and Dr. Reimann as the speakers.

Philadelphia

Society News.—Drs. Paul H. Langner Jr. and Richard A. Kern, among others, addressed the Philadelphia Allergy Society October 26 on "Studies on Local Reactions after Protamine Insulin Injections."—Drs. Josephine B. Neal, New York, and John S. Lockwood addressed the Philadelphia Neurological Society October 28 on "Treatment of Meningitis by Sulfanilamide" and "Sulfanilamide in Experimental Hemolytic Streptococcus Meningitis" respectively.—A joint meeting was held October 28 by the sections on research of the Philadelphia Academy of Stomatology and the Philadelphia County Dental Society; Philadelphia section, International Association for Dental Research and the section on stomatology, Philadelphia County Medical Society. Among the speakers were Drs. Guy M. Nelson, on "Influence of Focal Infection, Especially from the Teeth, on Cholecystitis"; John B. Ludy and Enayat Shirazy, D.D.S., on "Congenital Fistulae of the Lip."

State Takes Over Byberry Hospital.—The Philadelphia Hospital for Mental Diseases, commonly known as Byberry, was taken over by the state department of welfare October 22 in accordance with a law passed by a special session of the legislature and signed by Governor Earle September 30. The

transfer was delayed when a taxpayer's suit for an injunction was filed and the injunction granted in the Dauphin County Court. The injunction was later dissolved, the court stating that the complainant failed to show that he was seriously damaged by the transfer of the hospital to the state. Dr. Herbert C. Woolley, superintendent of the Pennhurst State School for the Feeble-minded, has been appointed superintendent, succeeding Dr. Wilbur P. Rickert. A building program amounting to \$7,500,000 has been proposed and now awaits approval for PWA funds to finance it. The transfer of the Philadelphia Hospital for Mental Diseases to the state climaxes a long series of investigations and exposés revealing serious overcrowding in the hospital. The Philadelphia *Record*, in a review of the situation, points out that the newspaper has made periodic investigations and has urged reforms for the past ten years. During the past year there have been investigations by a grand jury, by a committee of physicians and by a legislative investigating committee, finally resulting in legislative action. The hospital is said to have more than 5,600 patients in quarters originally built for 3,500. It will now be known as the Philadelphia State Hospital.

Pittsburgh

Society News.—Drs. Arthur B. Thomas and Leslie H. Osmond addressed the Pittsburgh Academy of Medicine October 11 on "Nature and Treatment of Edema" and "Silicosis and Silicosis with Infection" respectively.

Hospital News.—Mercy Hospital celebrated its annual "Mercy Day" September 22 with a clinic and a scientific meeting at which the speaker was Dr. William Boyd, Toronto, Canada, on "Bronchial Carcinoma."—Dr. Everts A. Graham, St. Louis, gave an address on "Malignant Tumors of the Lung" at the annual observance of "West Penn Day" at the Western Pennsylvania Hospital October 18.

TEXAS

Obstetricians and Gynecologists Meeting.—The Texas Association of Obstetricians and Gynecologists held its annual meeting in San Antonio September 24. Dr. Thomas Benton Sellers, New Orleans, delivered the J. F. Y. Paine address on "Hysterosalpingography—A Valuable Adjunct in Gynecological Diagnosis." Dr. Sellers also spoke at an evening meeting on sterility. Dr. Henry Reid Robinson, Galveston, was chosen president-elect and Dr. Joseph W. Bourland, Dallas, was installed as president. Dr. Roy L. Grogan, Fort Worth, was elected vice president and Dr. Minnie L. Maffett, Dallas, secretary, reelected.

Society News.—Drs. Howard O. Smith and Milton A. Davidson, Marlin, addressed the Hill County Medical Society, Hillsboro, September 9 on "Transvaginal Sterilization" and "Obstetrical Analgesia" respectively.—Among the speakers at a meeting of the Palo Pinto-Parker Counties Medical Society, Weatherford, September 6, were Drs. Platt L. Allen, Weatherford, and Joe H. McCracken, Mineral Wells, on "Pertussis" and Roy L. Grogan, Fort Worth, "Dermatologic Problems of the New-Born."—Drs. Rollin S. Fillmore Jr., Jacksboro, and Harold L. Warwick, Fort Worth, addressed the Tarrant County Medical Society, Fort Worth, September 6, on "Varicose Ulcer—Pathogenesis and Rationale of Treatment" and "Otosclerosis" respectively.—Drs. Rufus L. Powers and John Valton Sessums, San Angelo, addressed the Tom Green-Eight County Medical Society September 6 on "Scarlet Fever" and "Carcinoma of the Rectum" respectively.—Dr. James T. Robison Jr., Austin, and W. B. McCall, D.D.S., Temple, addressed the Williamson County Medical Society, Georgetown, September 13 on "Sinusitis in Relation to Cough" and "Focal Infection in the Mouth" respectively.

WASHINGTON

Executive Secretary for State Society.—Mr. Jack M. Geoffroy, Topeka, Kan., recently associated with the research department of the Legislative Council of the State of Kansas, has been appointed executive secretary of the Washington State Medical Association, according to *Northwest Medicine*. Mr. Geoffroy graduated from Washburn College, Topeka, Kan., in 1934 and has been with the Legislative Council since that time.

WEST VIRGINIA

Special Society Meetings.—Dr. George F. Evans, Clarksburg, was reelected president of the West Virginia Tuberculosis and Health Association at the annual meeting in Huntington September 27-28. Among the speakers at the meeting were Drs. Anthony V. Cadden, Hopewell, on "Results of Modern

Methods of Sanatorium Treatment"; Donald L. Butterfield, Charleston, "Medical and Social Problems of Tuberculosis in the Relief Program," and George H. Barksdale, Charleston, "What Parents Should Be Told About Tuberculosis."—The fall meeting of the West Virginia Heart Association was held in Huntington October 13. Guest speakers who conducted clinics and gave addresses were Drs. Samuel Brown, Cincinnati, on "Roentgenologic Diagnosis of Heart Disease"; Julien E. Benjamin, Cincinnati, an electrocardiographic slide demonstration, and Arthur Carlton Ernsteine, Cleveland, "Common Errors in Cardiac Diagnosis." At a joint meeting with the Cabell County Medical Society and the West Virginia fellows of the American College of Physicians in the evening Dr. Claude S. Beck, Cleveland, spoke on "Surgery of the Heart."

WISCONSIN

Orthopedic Clinics.—The Sheboygan County Medical Society and the crippled children division of the state department of public instruction sponsored an orthopedic clinic in Sheboygan September 24. Drs. Henry L. Greene, Madison, and Ralph M. Carter, Green Bay, examined the children; members of the staff of the Sheboygan Orthopedic School and the crippled children division assisted in taking histories and interviewing parents. The Eau Claire-Dunn-Pepin County Medical Society sponsored a similar clinic October 12.

Option on Surgeons' Quarters at Old Fort.—Efforts are being made by the Wisconsin Daughters of the American Revolution to restore an old building used as surgeons' quarters at Old Fort Winnebago near Portage. The fort was built in 1828 and evacuated twenty years later. For several years the buildings were under the care of a watchman but they were finally sold. Now all the buildings have vanished except the surgeons' quarters, which is "the birthplace of medicine in central Wisconsin," according to the *Wisconsin Medical Journal*. The Wisconsin organization is seeking funds to purchase and restore the building, on which it has an option.

Society Awards to Drs. Carey and Middleton.—The State Medical Society of Wisconsin at its annual meeting in Milwaukee in September presented the Council Award, a gold seal of the society, to Drs. Eben J. Carey, dean, Marquette University School of Medicine, Milwaukee, and William Shainline Middleton, dean, University of Wisconsin Medical School, Madison. Dr. Carey was honored for his "high accomplishments in medical education and research" and for his "perfection of the art and dynamic use of visual education as a means of furthering the health of our citizenry." The seal was awarded to Dr. Middleton, according to his citation: "for accomplishments and lofty inspiration in the teaching of students and practitioners, for your quarter of a century of public service and for your outstanding influence in the development of a high quality of medical service for the citizenry of Wisconsin." The gold seal has previously been awarded to twelve physicians.

GENERAL

Meeting of Military Surgeons.—The forty-sixth annual meeting of the Association of Military Surgeons was held at Rochester, Minn., October 13-15 under the auspices of the Mayo Clinic and Foundation. The speakers included: Capt. George W. Calver, U. S. Navy, Washington, D. C., "Is America Physically Fit for War?" Brig. Gen. Leigh Fairbank, D. C., U. S. Army, Washington, Dental Aspects of Preventive Medicine. Ralph Creer, senior clinical photographer, research department, Veterans' Administration, Hines, Ill., "Clinical Photography in the U. S. Army." Lieut. Comdr. Charles H. Watkins, U. S. N. R., Rochester, Minn., "Recent Advances in the Field of Blood Dyscrasias." Dr. John S. Lundy and Lieut. Lloyd H. Mousel, medical reserve, U. S. Army, Rochester, "Present Status of Anesthesia and Its Practical Application in the Combat Zone." Lieut. J. Grafton Love, Rochester, "Low Back and Sciatic Pain Due to Protruded Intervertebral Disks." The program at the banquet Friday evening was in honor of Rear Admiral Perceval S. Rossiter, surgeon general of the U. S. Navy, who will reach the retirement age November 30. Col. George E. Ijams, Veterans Administration, Washington, discussed "America's Problem." Dr. Thomas Parran, surgeon general of the U. S. Public Health Service, Washington, D. C., was elected president; Major Gen. Charles R. Reynolds, surgeon general of the U. S. Army, Washington, and Drs. Harold D. Corbusier, Plainfield, N. J., James A. Mattison, Los Angeles, and William L. Mann, San Diego, Calif., were elected vice presidents. The 1939 meeting will be in Washington.

Society News.—Dr. Everett Morris, Auberry, Calif., was elected president of the American Academy of Tuberculosis Physicians at the annual meeting in San Francisco recently.

Drs. Benjamin P. Potter, Secaucus, N. J., and John B. Crouch, Colorado Springs, were elected vice presidents and Dr. Arnold Minnig, Denver, secretary.—Dr. Fred G. Carter, Cincinnati, was chosen president-elect of the American Hospital Association at its recent annual meeting in Dallas, Texas, and Dr. George Harvey Agnew, Toronto, Canada, was installed as president. The 1939 meeting will be in Toronto.—Dr. Hyman I. Spector, St. Louis, was elected president of the Mississippi Valley Conference on Tuberculosis at its annual meeting in St. Louis September 23; W. P. Shahan, Springfield, Ill., executive secretary of the Illinois Tuberculosis Society, was chosen vice president, and A. W. Jones, St. Louis, was reelected secretary-treasurer.—Dr. George P. Muller, Philadelphia, was chosen president-elect of the American College of Surgeons at the annual session in New York October 17-21. Drs. Henry W. Cave, New York, and David E. Robertson, Toronto, were elected vice presidents.

American Congress of Obstetrics and Gynecology.—Plans are in the making for the first American Congress on Obstetrics and Gynecology to be held in Cleveland Sept. 11-15, 1939. The scope of this congress has been extended beyond that of similar assemblies in the past and will include not only medical groups but those devoted to nursing, public health and institutional administration. National sectional and local societies have approved the congress and have contributed to its support. It is now desired, the announcement says, to obtain a wider representation through the medium of contributing memberships at \$5 each. Application for these memberships may be made at the office of the congress, 650 Rush Street, Chicago. In addition to scientific sessions it is planned to provide several evening meetings at which speakers of prominence will address the public. There will also be a comprehensive exhibit, scientific, educational, technical and commercial. The American Committee on Maternal Welfare, which includes in its membership twenty organizations interested in the subject, has been delegated to sponsor the congress. The members of the executive committee in charge of arrangements are Dr. Fred L. Adair, Chicago, general chairman; Dr. Robert D. Mussey, vice chairman, Rochester, Minn.; Miss Sara B. Place, Chicago, secretary; Dr. Rudolph W. Holmes, Chicago, treasurer, and Dr. Frederick H. Falls, Chicago, assistant treasurer.

Southern Medical Association.—The thirty-second annual meeting of the Southern Medical Association will be held in Oklahoma City November 15-18 under the presidency of Dr. James W. Jervy, Greenville, S. C. Tuesday November 15 will be Oklahoma City Day, when general clinical sessions will be held on medicine, surgery, gynecology and obstetrics. Tuesday evening there will be a general public session with the following speakers:

Dr. Irvin Abell, Louisville, Ky., President of the American Medical Association, "The Role of Surgery in Fighting Disease."
Dr. Thomas P. Sprunt, Baltimore, "Diet Fads, Foods and Vitamins."
Rev. Alphonse M. Schmitt, St. Louis, "Society's Debt to the Doctor."
At a general session Wednesday evening Dr. Jervy will deliver his presidential address, entitled "Ars Medica and Ars Poetica." Among speakers who will address the numerous section meetings will be:
Dr. Russell L. Haden, Cleveland, "Treatment of Rheumatoid Arthritis."
Dr. Henry F. Helmholz, Rochester, Minn., "The Role of Stasis and Infection in Renal Insufficiency of Later Life."
Dr. Jacob Arnold Bergen, Rochester, Minn., "Causes of Colonic Cancer: Clinical Support of Current Hypotheses."
Dr. William C. Menninger, Topeka, Kan., "Psychoanalytic Principles in Psychiatric Hospital Therapy."
Dr. Robert D. Schrock, Omaha, "Bone Tumors."
Dr. Charles O. McCormick, Indianapolis, "Analgesia in Labor: Modified Gwathmey Technic."
Dr. Dudley A. Smith, San Francisco, "Management of Complex Fistula in-Ano."
Dr. Edward C. Holmblad, Chicago, "Improved X-Ray Technic in Studying Knee Joints."
Dr. Bernard Samuels, New York, "Pathology of Complicated Cataracts."

Other groups that will meet during the week are the southern branch of the American Public Health Association, National Malaria Committee, American Society of Tropical Medicine, Southern Association of Anesthetists and region 2 of the American Academy of Pediatrics.

Warning—Fraudulent Magazine Solicitors.—The Professional Sales Corporation, New York, reports that one John Bowles, formerly employed by the corporation, is still taking unauthorized subscriptions for various magazines, using both his own name and the alias of John Hamilton. His activities have recently been reported from physicians in Montgomery County, Ohio. The corporation wishes to warn physicians to beware of this impostor and is making every effort to apprehend him. A warning was published in *THE JOURNAL* July 9.

—The National Publishers Association, New York, reports the fraudulent activities of an agent using the name H. E. Stanton. It is said that this man has operated throughout the country and has victimized physicians exclusively. At one time he was employed by Preferred Publications, Inc., a reliable agency in New York, and absconded with a supply of its order forms. He solicits subscriptions to any and all magazines, many of which the agency does not represent, pockets the full amount of his collections and makes no report of orders to the agency. On some of these orders he has promised a \$10,000 accident and travel policy as a premium. He has been in the Southern states, worked his way up the states on the Mississippi River, then castward and was last heard of in Boston. Physicians are warned to look for this man and avoid any dealings with him. His description is as follows: aged about 38; 5 feet 8 inches tall; weighs about 135; has gray eyes, dark brown hair and fair complexion.

American Public Health Association Meeting.—The American Public Health Association at its sixty-eighth annual meeting in Kansas City, Mo., October 25-29, dealt, in addition to its usual scientific program, with the subject of expanded facilities for public health and proposed plans for medical care as outlined in the proposals of the Technical Committee, as presented to the National Health Conference held in Washington in July. The principal speakers were Dr. Thomas Parran Jr., surgeon general of the United States Public Health Service, Washington, D. C.; Abel Wolman, Dr. Eng., president-elect, Baltimore; Arthur J. Altmeyer, chairman of the Social Security Board, Washington, D. C.; Dr. Irvin Abell, President of the American Medical Association, Louisville, Ky., and Prof. Charles E.-A. Winslow of Yale University, New Haven, Conn. Dr. Parran supported the proposals of the National Health Conference and expressed his appreciation of the support given to these proposals, with certain exceptions, by the House of Delegates of the American Medical Association. Dr. Wolman in a somewhat satirical vein intimated that the United States is a century in arrears in public health development, grudgingly conceded that the American Medical Association supported the proposals of the National Health Conference in the main, and intimated that the support was reluctant and tardy. Mr. Altmeyer made a straightforward presentation of the aims of the National Health Conference and outlined the methods by which it was proposed to arrive at the objectives. He emphasized that progress was to be made through state plans and developments with the federal government cooperating principally through furnishing financial grants in aid and technical services. Dr. Abell described the experimentation already carried out by the medical profession in the field of medical care and hospitalization, as well as its traditional support of public health measures. He then set forth the actions of the House of Delegates of the American Medical Association at the special session, September 16 and 17, reading the committee reports verbatim and almost without comment. Professor Winslow, ostensibly speaking for the consumer of medical services, reiterated the familiar arguments about lack of medical care for certain groups in the United States, ridiculed statistical studies other than those in support of his thesis, and attacked the organization and policies of the American Medical Association. In substance he declared that the American Medical Association would never function effectively on the basis of its present organization and should be reorganized on what he termed "a service basis," namely with the hospital as the functional unit of organization instead of the county medical society. He praised the "independent" Committee of Physicians.

The following resolutions were passed by the association:

The American Public Health Association, ever increasingly conscious of the leadership and competence which have characterized the work of the various Federal health agencies, records its unanimous satisfaction in the further evidence of the effective interest of the Federal government in the health of the Nation, embodied in the recommendations of its Interdepartmental Committee to Coordinate Health and Welfare Activities to the National Health Conference, July 18-20, 1938.

There can be no doubt that large areas of many of our States do not enjoy the benefits of adequate health service. We maintain that without adequate local health organization covering every area of the United States, the delivery of the full benefits of modern public health procedure to all the people in the United States cannot be accomplished. We recognize further the indispensable services which State departments of health are capable of contributing over and above those provided under local governmental units in urban or rural communities.

In recognition of these facts, we endorse the recommendations presented before the National Health Conference by the Technical Committee on Medical Care, which propose the expansion of public health services, including necessary medical, hospital and nursing care for the period of maternity and childhood in families unable to obtain adequate care through their own resources.

An appraisal of national health resources reveals the existence of many communities in which hospital facilities are meager or lacking. The inadequacy of institutional facilities presents a handicap to the control of tuberculosis and mental disease, and deprives those requiring care in general hospitals of the full benefits of modern medical treatment. In certain communities adequately supplied with hospitals, economic barriers prevent their full utilization. For large numbers of our population, inadequate income results in inadequate medical and dental care. The concept of the close interrelation of preventive and curative medicine is basic to the modern public health program.

We therefore endorse the recommendations of the Technical Committee to the National Health Conference providing for Federal aid to the States for the construction of additional hospital facilities, the provision of essential medical and nursing care, and hospital care as required, to persons unable to support such care from their own resources, and the compensation against wage loss incurred through sickness. In connection with the Technical Committee's recommendation concerning medical care, the Association supports the view that in the initiation and development of the program, wide latitude should be given to the States in the definition of the population to be served and the method of providing medical service.

We pledge the American Public Health Association to use all its professional resources, and such influence as it has earned through sixty-eight years of development and leadership in Public Health to aid governmental agencies in accomplishing these statesmenlike health objectives.

Furthermore, we offer our cooperation to the governmental agencies which may be charged with the proposed expansion of health services in the United States, and we stand ready to collaborate with other professional and scientific organizations having similar principles and objectives, to the end that at the earliest possible date in every area under the jurisdiction of the United States the whole population may have the benefit of the best that public health service can bring them.

Be it Resolved, That the foregoing declaration expresses the formal and considered opinion of the American Public Health Association and that it shall be published in the *Journal*. *Be it further*

Resolved, That the Executive Board is hereby instructed to appoint a representative committee of seven Fellows of the Association to cooperate during the coming year with the Interdepartmental Committee of the United States Government, with the American Medical Association, the American Dental Association, National Organization for Public Health Nursing, the Conference of State and Territorial Health Officers, and with other agencies, to the end that these principles may be translated into effective action.

The most significant difference between the expressions of speakers on the association program and the resolutions as adopted will be found in the silence of the resolutions relating to the question of medical care beyond the statement that "in the Technical Committee's recommendation concerning medical care the association supports the view that in the initiation and development of the program wide latitude should be given to states in the definition of the population to be served and the method of providing medical service."

The following additional resolution was passed:

The American Public Health Association records its appreciation of the participation in its deliberations during this Annual Meeting week of Dr. Irvin Abell, President of the American Medical Association. It records with pleasure its agreement with the approval in principle, at a recent special session of the House of Delegates of the American Medical Association, of the content of the national Health program presented by the Interdepartmental Committee to the National Health Conference. The Association pledges its continued cooperation and support to the American Medical Association in the translation of this policy into action.

Press comment on the meeting was a little confusing. The *Kansas City Times*, October 28, carried a front page story under the headline "For Health Plan: Program Including Compulsory Insurance Endorsed by Public Health Association: Calls for 850 Million: Rift with American Medical Group Which Had Declined to Back Proposal." The story under these headlines declared "In giving approval to the health insurance plan, the association moved further away from the traditional leadership of the American Medical Association." In the *Kansas City Star* of the same date a statement appeared by Dr. Arthur T. McCormack, president of the American Public Health Association, in which he called attention to the fact that the association "by leaving reference to it out of the resolution did not grant approval to the compulsory medical insurance plan of the National program." The *Kansas City Journal* carried a story headlined "Health Experts Silent on Forced Insurance Plan But Follow Lead of A. M. A. on Four Other Planks."

CORRECTION

The Nature of the Bleeding in Jaundice.—In the article by Dr. Armand J. Quick of Milwaukee in *THE JOURNAL*, May 14, the directions for the preparation of the calcium chloride solution in the section on the quantitative determination of prothrombin (page 1659) should read as follows: Dissolve 1.10 Gm. of anhydrous chemically pure calcium chloride in 400 cc. of distilled water.

Foreign Letters

LONDON

(From Our Regular Correspondent)

Oct. 15, 1938.

Chronic Pneumonia

While chronic pneumonia is well known as a pathologic process, the textbooks do not recognize it clinically. At the Royal Society of Medicine, Dr. J. G. Scadding pointed out that in the nineteenth century great clinical interest was displayed in chronic pneumonia. Laënnec in 1826 described chronic pneumonia following acute pneumonia. Later writers disputed whether chronic indurative pneumonia began with an acute phase. In 1936 Scadding described three cases as "chronic diffuse bronchopneumonia," which ran a chronic course of two years, seven months and three and one half years, respectively, to a fatal termination and simulated pulmonary tuberculosis both clinically and radiologically. At necropsy the essential lesion was a pneumonia in widespread foci showing an unusual variety of modes of progress and spread. Scadding's paper was based on eight cases seen at the Hospital of the British Postgraduate Medical School.

CHRONIC CIRCUMSCRIBED NONSUPPURATIVE PNEUMONIA

The usual type of delayed resolution of acute pneumonia falls in this group. While resolution of lobar pneumonia is usually complete in two or three weeks from defervescence, radiologic studies show that complete clearing of opacities may be much delayed—for as long as eighty-five days in one case. Since complete clearing without gross fibrosis is possible, no organization and little suppuration must take place. A similar condition of subacute or chronic consolidation, capable of complete resolution, can arise insidiously or with only mild symptoms at the onset. When it persists for a long time a confusing clinical picture is presented, as in the following case:

A clerk, aged 56, was admitted with a history of increasing weakness and lassitude for eighteen months, loss of more than a stone (6.35 Kg.) and more acute symptoms for seven days, starting with aching in the limbs and one attack of vomiting and cough, mainly unproductive. On admission he was afebrile and he remained so. He looked pale and ill. There was dyspnea on slight exertion. There was diminished movement of the right side of the chest with dulness posteriorly, and weak breath sounds, bronchial in character, in the interscapular region. The scanty sputum was negative for tubercle bacilli; a very mixed flora was found, including coarse spirochetes and fusiform bacilli. X-ray examination showed restriction of movement of the right diaphragm and slight displacement of the mediastinum to the right. Extending out from the right hilar region was an irregular shadow, mainly posterior. Bronchoscopy revealed a normal bronchial tree. A pulmonary growth was suspected. Eight weeks later he was much improved, but the pulmonary signs remained of the same type but were diminished. Three months still later there was complete clearing, and eventually he completely recovered. Chronic suppurative pneumonia may take place with or without abscess formation.

London's Preparations for Air Raid Casualties

In previous letters some of the extensive preparations made in London for dealing with air raid casualties have been described. The elaborate scheme prepared by University College Hospital for dealing, if necessary, with 1,000 casualties

from one air raid was outlined. Further particulars can now be given for the rapid conversion of this hospital into a casualty clearing station. It was arranged to evacuate all the patients. Those who could not be taken to their homes were to be transported to Oxford. The hospital could thus have been emptied in a few hours. Detailed preparations were made for the reception and disposal of casualties. Even the administration of morphine in the darkness, in the event of the lights failing, had not been overlooked and syringes were prepared containing the appropriate doses. For dealing with the gas wounded alone there were twenty-one teams, each consisting of surgeon, assistant surgeon, two dressers and a nurse, working in four shifts. From forty to sixty gas cases could have been treated at one time. Arrangements were made for 100 blood transfusions a day, and there was a cold room for the storage of blood. The outstanding deliveries of medical supplies were called up, giving a three months' supply. The protection of the staff was arranged for in tunnels and basements and gas-proofed rooms, giving accommodation for 380. Places which had not been touched for years were cleared out by the students, giving bomb-proof shelters for 2,000 people.

This is an example of what was done at the great hospitals attached to London's medical schools. The municipal hospitals, which form the largest organization in the world and normally contain 36,000 beds, could coordinate their preparations, as they are all under the control of one authority, the London County Council. Their accommodation was increased by 20 per cent and they were supplied with additional drugs and dressings, estimated to meet the requirements for one month of an acute emergency period. A supply of antitetanus serum was received from the government. Ten of the fever hospitals were supplied by the Ministry of Health with surgical equipment for 5,000 beds. An additional 20,000 blankets were procured. Curtain material and fittings and neon lights were supplied to all hospitals for the purpose of "blacking out." A number of respirators, sufficient for all the patients and staff, candles and torchlights, sand, buckets and shovels to deal with fires from incendiary bombs, sandbags for the protection of vulnerable places, bleach powder for dealing with mustard gas, building materials for the protection of operating rooms, splints and dressings to meet a period of a three weeks emergency were supplied. The Ministry of Health sent 2,000 stretchers to those hospitals. Twenty-one ambulance trains, each with one doctor and seven nurses, were organized. Arrangements were made by which the hospital staffs would all be supplemented at a few hours notice by the allocation of all the school medical and nursing staff available. All the members of the clerical staff of the public health department who were not regarded as essential were allocated to the hospitals for any duties which the medical superintendents could provide. Arrangements were made by which seventy skilled surgeons and assistants would be available for staffing those fever hospitals which were to be upgraded into general hospitals. The result of all this would have been that on October 1 more than 16,000 beds would have been available in the municipal hospitals for the admission of the wounded.

Other preparations made by the London County Council included the addition of 420 units to the London fire department and volunteers to man the auxiliary service, earmarking of commercial vehicles for towing the trailer pumps, augmentation of the normal water supplies and keeping all potential supplies (swimming baths, ponds and the like) full of water. For the augmentation of the ambulance service some 2,000 vehicles and 5,000 women drivers were required. The ministry secured the vehicles, and the need for drivers was being advertised during the crisis.

PARIS

(From Our Regular Correspondent)

Oct. 6, 1938.

A Symposium on Bone Grafts

The second question to be discussed at the recent International Surgical Congress was "Bone Grafts," the first paper being read by Professor Cuneo of Paris. Opinion was unanimous that the best results followed the use of autoplasmic grafts but that success depended on the condition of the bone in which the graft was to be placed. This signified that the bone in which the graft is inserted must possess sufficient regenerative power to form new bone, the graft acting only as a stimulant. Homoplasmic and heteroplasmic bone grafts are far inferior to the autoplasmic variety. Success depends to a great extent on the age of the patient. In children and adults below 50 and in good general condition the chances of a successful outcome are excellent.

Dr. Albert of Liège, Belgium, spoke on the biology of bone grafts, emphasizing that the bone graft per se disappears either partly or completely and is replaced by newly formed bone. In following the laws of osteogenesis in general, the bone graft is an essentially vital phenomenon in which the cells hereditarily destined to form bone play the most important part. The conditions to be fulfilled to have a successful result are to prepare the bed in which the graft is to be placed in such a manner that the tissues forming the bed can give rise to osteogenic buds rapidly; to conserve the periosteal, cortical and medullary portions of the bone constituting the bed; to remove the graft with periosteum intact by mechanical means which do not destroy the vitality of the graft; to prepare the bed before attempting to remove the graft and finally to attempt to stimulate the cellular elements composing the bed by using perhaps in the future the two-step method suggested by Brooks. If these conditions are complied with, the living bone graft is the method of choice. The best chances of survival of the graft are to be expected if thin osteoperiosteal grafts are used as proposed by Ollier and Delagénière when smaller defects need to be filled and the Albee type of graft for larger ones. The latter method will yield more rapid results if early movement is desired.

Dead bone (as suggested by Orell) which has been previously subjected to physicochemical procedures and does not contain any osteogenic element only plays the part of a foreign body which is absorbable and simply acts as a splint until new bone formation has taken place. As all osteogenesis must originate in the osseous tissue around the bed in which any graft is placed, such specially prepared dead bone, termed "os purum," cannot be used when a large graft is called for. Such an objection also holds true for the other type of bone graft, the so-called os novum, as suggested by Orell. This "os novum" is obtained by inserting a particle of the "os purum" beneath the periosteum of the tibia, representing in reality a living graft. Whether one uses a living bone graft or one in the form of the "os novum" of Orell, success depends entirely on the osteogenic cells, no matter whether they have their origin in the graft itself or in the bed in which it is placed.

Professor Demel of Vienna read a paper on the results of bone grafts in recent bone injuries and pseudarthroses. In recent fractures, especially those due to gunshot or similar modes of injury, bone grafting is rarely indicated. In certain comminuted fractures when good reduction of fragments is impossible or there is a likelihood of the occurrence of a secondary pseudarthrosis, bone grafting is indicated provided one is sure that the bed is not infected. In pseudarthroses when there is a considerable loss of bone tissue the preferable method of treatment is to remove all cicatricial tissue after curetting the medulla of the two bones forming the pseudarthrosis and then transplant some free bone fragments containing both

periosteum and compact bone. The use, in addition, of some type of external bone splint is indispensable to assure good fixation of the grafts.

Mr. Platt of Manchester, England, said that he prefers some type of metallic bone splint in fractures to bone grafts. Pseudarthroses should not be operated on too early. Quite frequently simply curetting the ends of the bone and inserting a few osteoperiosteal bone fragments would suffice. If this method did not succeed he preferred a graft taken from the tibia at least for pseudarthroses in the long bones. He had found the shafts of the femur and the lower third of the tibia and of the humerus very unfavorable for bone grafting.

The next speaker was Dr. Svante Orell of Stockholm, who read a paper on the use of the bone graft in tuberculosis of the bones and joints. The "os purum" and "os novum" types of grafts, which he was the first to advocate, had many advantages over the living bone transplant. These newer types of grafts appeared to stimulate not only new bone formation but also the adjacent soft tissues. The "os purum" graft is dead bone which has been deprived of its fats, albuminoids and fibrous tissue by physicochemical procedures. The "os novum" is veritable new-formed living bone obtained by subperiosteal implantation of the os purum. He cited, illustrated by slides, a large number of cases in which these new types of bone grafts had been used in arthrodeses and in tuberculosis of the hip and spine.

The next paper was read by Dr. D. B. Phemister of Chicago on bone grafts in osseous dystrophies and tumors. He cited five personal observations, four of medullary sarcoma and one of cortical sarcoma, which had been treated by resection and bone graft. In two cases involving the upper end of the humerus, one had shown no evidence of recurrence since operation, two and a half years ago; the other had a fracture of the graft and recurrence fourteen months after operation. One case of sarcoma of the ulna had been apparently cured for four and a half years; death occurred in the other of metastases after two and a half years. In the fifth case, a sarcoma of the upper end of the femur, necessitating disarticulation at the hip and insertion of a bone graft from the tibia to give support for an artificial limb, operation was performed five months ago. Benign tumors and bone cysts are favorable cases for operation followed by use of a bone graft, unless there has been a large loss of bone. Two cases, one of the humerus, the other of the radius, of giant cell sarcomas were reported without recurrence for eighteen and twenty-five years respectively. In two cases of bone cyst of the femur no recurrence can be found following removal, thirteen and eight months respectively after operation.

Professor Kappis of Würzburg, Germany, reported a large number of cases in which bone grafts had been employed for chronic (nontuberculous and nonmalignant) arthropathies. He had successful results in 90 per cent of about 500 cases, such as grafts to immobilize the sacro-iliac joint, coxofemoral arthrodesis and fracture of the neck of the femur.

In the discussion of this series of papers, Dr. Danis of Brussels stated that the "os purum" graft of Orell is not as well tolerated as is a metal splint and is expelled after a relatively short interval. It does not possess any osteogenic property but nevertheless it is so easily employed that he has made use of it in many recent complicated fractures as well as in pseudarthroses.

Professor Lambotte of Antwerp, Belgium, prefers a metallic splint for pseudarthroses of the humerus and femur, limiting use of the bone-graft to pseudarthroses of the bones of the leg, forearm and clavicle. He believed that a bone graft inserted into the medulla of the ends of the bones does more harm than good, because in case infection supervenes it will be necessary to resect a considerable length of the end of the bones.

Dr. Clery of Chambéry, France, had employed dead bone in forty-eight cases of chronic painful arthritis of the hip with highly satisfactory end results.

Dr. Hybbinette of Stockholm reported six cases of resection of the lower jaw for tumor in which he had filled the defect with a graft taken from the crest of the ilium, a case which is especially adapted for such a graft.

Dr. André Richard of Paris and Berck-Plage, France, prefers living bone grafts and has never used metallic splints in 800 cases of tuberculosis of the spine and in 500 cases of tuberculosis of the hip.

BERLIN

(From Our Regular Correspondent)

Sept. 26, 1938.

The Fate of Austrian Scientists

A previous letter (*THE JOURNAL*, June 11, p. 2020) contained an account of the German government's new far-reaching legislation for the erstwhile Austrian state. In the meantime more details of the consolidation of the country since its annexation have been forthcoming and it is possible to report on the fate of many distinguished scientists under the new régime. Through the political upheaval the world famous Faculty of Medicine of Vienna University has suffered severe losses. It is estimated that about half of the assistant professors and instructors holding office at the time the Austrian republic was absorbed by the German reich have lost their positions. The Jewish element has been prominent among these groups whereas but few Jews have served as full professors (*ordinarien*) in recent years.

The following items concern some of the better known faculty members: Prof. Egon Ranzi, *ordinarius* in surgery and son-in-law of the Viennese surgeon Anton Eiselsberg, has been forced to relinquish the directorship of the university's surgical clinic and has been retired on a pension because he had been an adherent of Schuschnigg. Profs. Leopold Arzt and Wilhelm Kerl, both of them "Aryans" and ranking dermatologists, met the same fate as Ranzi for like reasons. Professor Arzt, decided anti-Semite, ardent proclerical and nephew of a late archbishop of Vienna, was in custody for a short time. Ernst P. Pick, professor of pharmacology and a pupil and successor of H. H. Meyer, was forced to retire on account of being a Jew. The physiologist Arnold Durig was also retired for reasons unknown.

As is generally known, Prof. Otto Loewi of Graz, who not long ago shared the Nobel prize with Sir Henry Dale of London, has been deprived of his post and spent some time in custody; he has lately been given his freedom. One of the younger psychiatrists, Prof. Otto Kauders, also of Graz, has been dismissed, ostensibly on racial grounds. Foremost among Viennese psychiatrists and neurologists to be affected by the new régime was Sigmund Freud, who has subsequently been received with great honors in London. Hans Hoff, one of the younger psychiatrists, has emigrated to the United States. Prof. Otto Marburg, *ordinarius* in neurology, has been deprived of his position; Erwin Stransky has suffered a like fate.

Among the internists who have lost their positions are G. Hitzengerger, radiologist; David Scherf, cardiologist; Julius Bauer, best known for his research on endocrinology and on constitution; Karl Glaessner, Otto Porges and Walter Zweig. The last named was a pupil of Ismar Boas. The tragic death of Professor Boas has previously been reported (*THE JOURNAL*, August 6, p. 550). The aged man had made Vienna his refuge from Nazi Germany. After the annexation of Austria he ended his life with an overdose of barbitol. Still other faculty members to be ousted were Moriz Oppenheim, dermatologist; Gottwald Schwarz, roentgenologist; Josef Friedjung, pediatrician; Richard Wagner and Heinrich Kahr, gynecologists, and Emil Froeschels, research phoniatician. Prof. Heinrich von Neumann, the otologist, a "non-Aryan," was under arrest until the successful intercession of his patient the duke of Windsor.

There have been other suicides in addition to Professor Boas: the aged pediatrician Prof. Wilhelm Knoepfelmacher; 74 year old Prof. Oskar Frankl, gynecologist, and the dermatologist Gabor Nobl, known for his injection therapy of varices. In view of the circumstances this report can make no claim to completeness. It does, however, provide an idea of how the change in the political status of Austria has affected faculties of medicine.

The Influence of Training on Skeletal Muscles

A. Hoffmann discussed the influence of training on the skeletal muscles before the Berlin Physiologic Society. The current view that muscle responds to any increased demand by hypertrophy is not substantiated by facts. Studies of athletic exercise have demonstrated that muscle adapts itself especially to the exercise by which it is developed; only increased demand within a given unit of time leads to effort hypertrophy, the sum of the exertion (continuous effort performance) having no part in it. According to the observations of Schiefferdecker each muscle possesses, peculiar to itself and to the animal species in question, a ratio of sarcoplasm to the fibrillary substance, size and number of nuclei and so on. This individual character of the muscle is determined by heredity but can be modified according to general health and the demands made on it by the individual. For example, the thickness of the fibers increases in the course of development, whereas the nuclear substance decreases. The microscopic observations of trained muscles are in part contradictory. Schiefferdecker noted in dogs which had undergone a continuous training an enlargement of the fibrous transverse section and a decrease in the number of nuclei; Thörner, on the contrary, in similar studies of dogs, observed no alteration in the thickness of the fibers but an increase in the number of nuclei. Siebert found that in rats forced to perform feats of strength in a definite time the skeletal musculature increased in weight and hypertrophy of the muscle fibers took place. Hoffmann himself performed experiments with thoroughbred Russian rabbits, with the following results: The effort required for different animals to run at various speeds varied greatly, but on the whole the training really amounted to a build-up of endurance. Each of a certain number of animals received, until completion of the experiment, 0.1 Gm. of caffeine per kilogram of body weight. The "caffeine rabbits" were obviously stimulated and displayed greater agility but became fatigued more quickly; these phenomena were particularly remarkable in the speedier rabbits. The spleens of the exercised rabbits were found to weigh in general considerably less than the spleens of the controls, but the spleens of the caffeine rabbits showed no diminution of weight. The hearts of exercised animals weighed more than the hearts of the controls; this increase was even conditioned to a certain extent by the distance traveled. Particular muscles examined were the biceps femoris, the gastrocnemius, the semitendinosus and the soleus. It was found that the muscles of the slow-running animals were always lighter than the muscles of the speedier animals and somewhat heavier than those of the controls; in any case the differences were slight. Increased thickness of the fibers was microscopically observed, together with marked decrease in the number of nuclei. The increase in transverse sections of fiber was accompanied by a corresponding decrease in muscle weight (in the slow-running animals). This phenomenon can be interpreted only by an increase in the muscle at the expense of the fat and of the connective tissue. The increased number of nuclei may be regarded as an economy of a muscle trained to endurance; this phenomenon corresponds with the greater economy of effort observed in other parts of the trained organism.

Prof. Friedrich von Müller 80 Years Old

Friedrich von Müller, who for many years served as *ordinarius* of internal medicine at Munich, celebrated his eightieth birthday, September 17. The occasion was recognized in all

scientific and academic circles of Germany. Müller is the last survivor of that group of illustrious men who a few decades ago dominated and determined the development of clinical medicine. Under their guidance the German clinic assumed a pre-eminent world role and the period of their leadership has already come to be regarded as classic. Friedrich von Müller, the son of a prominent Bavarian physician and hospital director, was during his student days particularly encouraged in scientific thought and endeavor by Carl Voit, one of the founders of classic metabolism. Müller received his clinical training from Carl Gerhardt in Würzburg and Berlin. Shortly thereafter Müller came to Bonn, as early as 1890 he was at Breslau as polyclinician, in 1892 he was appointed ordinarius at Marburg, in 1899 he became clinical ordinarius at Basel, and in 1903 he succeeded Ziemssen at Munich. His school years and wander years were productive of much work chiefly in the biochemical field: on the absorption of fat, on icterus and urobilin, on metabolism, on disintegration of protein in cancerous patients, on neurologic problems, on exophthalmic goiter, on diagnostic methods. This activity represented the beginning of a great and significant life work. Müller's teaching experience led him to write his famous "Taschenbuch der medizinisch-klinischen Diagnostik," a manual that reappears again and again in new editions and which for fifty years has been and still remains the matchless guide of each new generation of German physicians. This textbook owes its unique position not only to plenitude of material covered in it and the fact that frequent revisions have kept it abreast of contemporary knowledge but also to the extraordinary clarity of presentation. This clarity, this mastery of his subject matter, is notable throughout Müller's published work as well as in his lectures. He has often been invited to speak in foreign countries. His clinical lectures, his world-renowned courses in physical diagnosis always drew large attendance. Müller's lectures always had about them a sterling quality of excellence, they were always marked by a bold highlighting of the essential paths to be explored; he always arrived at the solution of a problem by accurate evaluation of various possibilities. Besides possessing all the qualities of a great physician, Müller has always been a fearless fighter. His impressive lineaments, sharp and angular as if hewn out of wood, are the outward expression of his character, his incorruptible loyalty to the right as he sees it.

BUDAPEST

(From Our Regular Correspondent)

Sept. 20, 1938.

The Medical Phase of Air Raid Precautions

Dr. Albert Telbisz, organizer of air raid precautions in Hungary, discussed at a recent meeting of the medical society the question as to who is available for medical service in case of gas attacks. Wearing a gas mask causes a change in the mechanism of respiration and circulation. The headband of a well fitting gas mask exerts pressure on the head and in certain persons circulatory troubles and headache supervene. The difficult breathing, profuse sweating, pain, limited sight and fright will disturb medical workers. In a gas-protecting dress the temperature and blood pressure rise, the pulse becomes accelerated, and the loss of body fluid is increased as the result of profuse sweating. The individual worker may collapse.

When a physician selects assistants he must examine them and declare only perfectly healthy subjects fit for air raid service. They must partake in air raid exercises to prepare themselves for this hard work. Some persons feel ill or collapse even during the exercises. This can be explained by the fact that, though they were found healthy, some circulatory disturbance may be latent which, owing to the great muscular effort necessary, suddenly causes decompensation. Dr. Telbisz had occasion to experience this in several cases. Therefore the medical examination should be thorough. When a gas mask is

being worn, respiration gradually becomes of the mouth breathing type, particularly if hard work is done; the mucous membrane dries and in consequence an upper prosthesis will fall down in the mouth and hinder breathing and eventually cause suffocation. Persons wearing prostheses should be instructed to take them out of the mouth.

In air raid precaution, physicians have to know what pathologic changes war gases produce in the nonprotected organism. From the pathologic picture he should quickly recognize what poison gas was used. This is important, as efficacious therapy depends on knowing the kind of gas present. There are war gases which produce symptoms that appear only after a latent period of several days. On the other hand, with other gases symptoms speedily supervene.

In planning to protect a hospital, it should be kept in mind that a hospital must always be capable of functioning during and after an aerial attack. A hospital must be independent of all public utilities, having its own water, gas and electric supply and also its own news service. The hospital must be prepared to treat a multitude of injured persons in an air raid. Oxygen inhalation apparatus and oxygen tanks should be handy, with a sufficient stock in storage. Persons exposed to mustard gas must be gas proofed first, and only afterward examined and treated, and gas-proofing stations must be erected within the hospitals.

It is a disputed question whether all hospitals in a threatened area should be evacuated. The answer, says Dr. Telbisz, is no, but only patients recently operated on and not easily transferable should be retained. Particularly important is the evacuation of hospitals which lie in the neighborhood of military barracks, post offices and telephone central exchanges, which will be attacked in case of air raids.

The war gases may affect also the drinking water and food. Water may be contaminated by mustard gas, and food can be soiled also by chlorpicrin. Drinking such water and eating such food may lead to serious consequences.

Telbisz finished his lecture by stating that to organize air raid defense is a difficult task for which experts are wanted.

Number of Diplomas in Hungary

The faculties of medicine of Hungarian universities issued in the school year 1913-1914 489 new medical diplomas, while in 1935-1936 they issued 398. Considering that in 1913 Hungary's population amounted to 18,000,000 while in 1936 it was only 9,000,000, the 398 diplomas issued in 1936 would seem excessive. In 1917 4,829 physicians practiced in Hungary, and in 1921, in the Hungary which has shrunk almost to one third of its former territory, just as many physicians are practicing. In spite of this, overproduction is not apparent, for now the number corresponds to a rate of one physician to 900 population, which rate would not be excessive if the physicians were better distributed from a geographic point of view. In Budapest itself the rate in 1920 was 1:420, while in 1936 4,460 physicians were registered at the Chamber of Physicians, corresponding to a rate of 1:239. In 1920 it was about 3,000 persons to one physician in the rural districts while in 1936 the number of rural physicians almost doubled and the rate became 1:1,412. In 2,317 of 3,374 villages there are no physicians. There are villages having a population of more than 3,000 with no physician.

In the cities, and especially in the capital city, the ever spreading sickness insurance endangers private practice. A grave problem is the question of free medical work. The reform of medical attendance on poor patients, contemplated by the ministry of health, will probably solve this question. The minister holds that a physician can work best only if his livelihood is assured, and therefore assuring their livelihood is no private affair of the medical profession but a public health matter. According to statistics issued by the bureau of taxa-

tion, of 8,451 practitioners 186 did not earn 200 pengos, or \$60; almost every fifth doctor earns less than 500 pengos, or \$150 yearly; 42 per cent did not reach 1,000 pengos yearly, or \$300, and only 28 per cent made 10,000 pengos, or \$3,000. The income of the most popular physicians did not exceed 60,000 pengos, or \$18,000. The so-called Aid for Young Physicians endeavors to deviate young doctors from the capital and to grant loans to village doctors until they can maintain themselves. These subsidies need not be repaid.

Typewritten Medical Prescriptions

The representatives of the Czechoslovakian Medical and Pharmaceutical Chambers discussed the problem of the legibility of medical prescriptions, since pharmaceutical chemists complained to the board that they often get prescriptions which are utterly illegible. As a consequence, the medical chambers require their members to write their prescriptions legibly. Those having such illegible handwriting must use typewriters.

ITALY

(From Our Regular Correspondent)

Oct. 1, 1938.

Meeting of Anesthetists

The Società italiana di anestesia e analgesia met recently in Bologna, with Professor Dogliotti as president. The first official topic was "Criteria for Selection of Anesthesia." Professor Gianotti concluded that preanesthesia is of value as complementary to ether and gas anesthesia. Basal (intravenous and rectal) anesthesia is of value but, in the majority of cases, cannot be a substitute for anesthesia by inhalation. Intravenous, rectal and chloroform anesthesia interfere with the functions of the liver and the kidney more than ether anesthesia. Use of the latter is especially indicated in children as well as in patients with syphilis, meningitis, mental or nervous disorders, infections with septicemia and shock. Ether and chloroform anesthesia aggravate acidosis. Gas anesthesia is harmless to the parenchymal organs. However, its administration is difficult because of the necessary apparatus and technic. Spinal anesthesia is contraindicated in hypotension as well as in all conditions in which ether anesthesia is indicated. Persons of the macrosplanchnic type tolerate spinal and peridural anesthesia better than those of other types. Peridural anesthesia is more advisable than high subarachnoid anesthesia. The latter, especially if nupercaine is used, may be followed by immediate or late complications. Nupercaine has to be used in small doses when it is used for local anesthesia in patients in poor nutritional conditions or in those who are suffering from pathologic conditions of either the liver or the kidney.

Professor Gosset reported satisfactory results from cyclopropane anesthesia in 467 cases. The toxicity of cyclopropane is low and when mixed with oxygen in the proportion of 22 per cent it induces anesthesia with loss of the reflexes. According to Wcese's opinion, based on results of experiments, the complications which follow operations on phlegmons of the mouth are caused by changes of respiratory reflexes which originate in the carotid sinus.

Professors Trincas and Oggioni reported experimental results obtained with Donaggio's method. Donaggio, in the course of the Congress of the Società di anestesia e analgesia which took place in 1936, said that he succeeded in showing the microscopic changes which anesthetic substances cause on the nerve fibers. He used a special method of fixation and coloration in making the microscopic preparations. The pathologic changes have the characteristics of the initial phase of primary degeneration. Professors Trincas and Oggioni studied, by means of Donaggio's method, the action of procaine hydrochloride, nupercaine, tutocain and prexocaine on the fibers of the cervical sympathetic. Procaine hydrochloride, nupercaine

and tutocain have a selective action on the neuraxis. Prexocaine attacks the myelinic sheath.

Professor Ruggeri made a chart on the gradation of changes induced by cocaine, stovaine (amylocaine hydrochloride, B. P.), procaine hydrochloride, tutocain and pantocain on the fibers of the sciatic nerve. The most grave changes are those induced by pantocain and procaine hydrochloride.

The second official topic was "Anesthesia with Heated Ether Vapor." Professor Parenti said that by heating ether vapors and administering them under high tension they acquire the characteristics of a gas less toxic and more active than ether. With D'Agostino's apparatus the patients inhale heated ether vapors and at the same time they inhale a mixture in which the amount of air, the expired carbon dioxide and the water vapor can be controlled. The speaker found, by clinical investigations, that heated ether vapors reach the respiratory tract of the patients at a temperature of 18 or 20 C. (64.4 to 68 F.). He found by experiments on animals that during administration of anesthesia by means of D'Agostino's apparatus the air is quickly regulated at the first segments of the respiratory tract and is maintained at a constant temperature in the tracheobronchopulmonary system. The speaker has found on microscopic study that normal ether vapors harm the respiratory tract more than the heated ones. The latter enter the blood in smaller proportions and are more quickly eliminated than the former. Professor Giordanengo showed a device of his own which can be attached to the common masks to obtain heating of anesthetic vapors.

Marriages

WILLIAM LARKIN NORVILLE, Whitmire, S. C., to Miss Lillie Mae Freeman of Rutherfordton, N. C., June 3.

WILLIAM BERTRAM MARTIN, Warrior, Ala., to Miss Emily Francis Johnson of Birmingham in August.

RAYMOND FRANCIS SMITH to DR. JANITH STEWART KICE, both of Garden City, N. Y., July 20.

SOL STEIN KAUFMAN, Rayne, La., to Miss K. Yelverton of Mize, Miss., at Bunkie, La., June 2.

JOHN K. BURNS, Spokane, Wash., to Miss Neva L. Palmer of Klamath Falls, Ore., August 25.

JOSEPH NAGLE, Portsmouth, Va., to Miss Jane Elizabeth Montgomery of Norfolk, July 19.

EDWARD A. KUEHN, Vandalia, Ill., to Miss Marguerite Robbie of Cedar Rapids, Iowa, August 8.

JOHN B. ALSEVEN, Syracuse, N. Y., to Miss Janet Gilbert of Springfield, Mass., August 27.

WILLIAM NILES WISHARD JR. to Miss Carolyn Louise Davis, both of Indianapolis, October 10.

MARSHALL H. AIZEN, Tiffin, Ohio, to Mrs. Hester Witbeck Ross of Sandusky, August 28.

THOMAS HAMILTON BREM, Baltimore, to Miss Emily E. Bloss of Roselle, N. J., August 27.

ALVA M. KIRKPATRICK to Miss Esther Whitson, both of Columbus, Ind., in August.

RICHARD VAN DYCK KNIGHT to Miss Janc Wyeth, both of New York, September 3.

CHARLES J. KISTLER, Kingston, Pa., to Miss Marjorie Bone of Nanticoke, June 12.

HARVEY G. E. MALLOW to Miss Alice Dierker, both of Watertown, Wis., July 21.

JOHN M. BRECHT to Miss Margaret R. Shank, both of Norristown, Pa., June 18.

JOSEPH L. KRUSZEWSKI to Miss Sophie Taczala, both of Milwaukee, July 6.

WILLIAM H. FRACKELTON to Miss Janc Love, both of Milwaukee, June 18.

RAYMOND J. KOKOWICZ to Miss Irene R. Rozycki, both of Detroit, in June.

ROBERT J. PORTER to Miss Jean Beycr, both of Des Moines, Iowa, June 16.

Deaths

Henry Martyn Bracken ☉ secretary and executive officer of the Minnesota State Board of Health from 1897 to 1919, died, September 25, at his home in Claremont, Calif., of chronic myocarditis, aged 84. Dr. Bracken was born in Noblestown, Pa., Feb. 27, 1854. He received the medical degree from the College of Physicians and Surgeons, Medical Department of Columbia College, New York, in 1877, and was a licentiate of the Royal College of Surgeons of Edinburgh, Scotland, in 1879; then for three years he was a ship surgeon. On the organization of the Medical College of the University of Minnesota in 1887 Dr. Bracken was appointed professor of materia medica and therapeutics. He lectured on public health and preventive medicine and for a time was acting dean of the medical college from which he resigned in 1907 to give his time to the state board of health. Dr. Bracken was appointed a member of the state board of health in 1895 and was elected secretary and executive officer in 1897. In 1902 he was president of the Conference of State and Provincial Health Authorities of North America and from 1908 to 1913 secretary-treasurer. He was a member of the first board of directors of the National Tuberculosis Association. In 1906 he organized the Minnesota Association for the Prevention and Relief of Tuberculosis, now the Minnesota Public Health Association. He also organized the Minnesota State Sanitary Conference and was its secretary. In 1919, Dr. Bracken was commissioned in the reserve corps of the United States Public Health Service as surgeon and was assigned to the Veterans' Bureau. He resigned in 1923. He was a member of the Minnesota State Medical Association, International Congress of Hygiene and Demography, International Congress of Tuberculosis, Royal Sanitary Institute, England, and the American Association for the Study and Prevention of Infant Mortality, honorary vice president of the fourth International Congress on School Hygiene and past president of the American School Hygiene Association. He was at one time attending physician to the Asbury Hospital and St. Barnabas Hospital in Minneapolis. Dr. Bracken was secretary of the Section on Hygiene and Sanitary Science of the American Medical Association, 1901-1902, and chairman, 1902-1903, and member of the Council on Health and Public Instruction from the time of its organization in 1910 until the 1919 session.

John Roberts Caulk ☉ St. Louis; Johns Hopkins University School of Medicine, Baltimore, 1906; professor of clinical genito-urinary surgery, Washington University School of Medicine; member of the Southern Surgical Association and the Clinical Society of Genito-Urinary Surgeons; past president of the American Urological Association and the American Association of Genito-Urinary Surgeons; fellow and member of the board of governors of the American College of Surgeons; served in various capacities on the staffs of the Barnes Hospital, St. Louis Maternity Hospital, St. Luke's Hospital, St. Louis Children's Hospital, Jewish Hospital, Evangelical Deaconess Home and Hospital and St. Louis County Hospital; contributor of chapters to Cabot's "System of Urology," Bartlett's "Post-Operative Surgery," Lewis' "Surgery" and "Cyclopedia of Practical Medicine"; aged 56; died, October 13, in Clayton, Mo.

Alexander Fraser, New York; Dalhousie University Faculty of Medicine, Halifax, N. S., Canada, 1897; member of the Medical Society of the State of New York; formerly professor of pathological histology at the University and Bellevue Hospital Medical College, and professor of pathology and bacteriology at the New York Polyclinic Medical School and Hospital; pathologist to St. Vincent's Hospital, consulting pathologist and bacteriologist to the New York Polyclinic Hospital, consulting pathologist at the New York Foundling Hospital, and the Manhattan Maternity Hospital, New York, and the Monmouth Memorial Hospital, Long Branch, N. J.; aged 69; died, September 18 at his summer home in Beechurst, L. I., of acute cholangitis.

Arthur Everett Austin, Boston; Harvard University Medical School, Boston, 1887; fellow of the American College of Physicians; professor of theory and practice of medicine, emeritus, Tufts College Medical School; formerly professor of biochemistry at the University of Virginia, and the University of Texas, Galveston; formerly on the staffs of the Mount Sinai Hospital and the Massachusetts General Hospital; served during the World War; author of "Manual of Clinical Chemistry" and "Diseases of the Digestive Tract and Their Treatment"; aged 77; died, August 22, in Windham, N. H.

Harvey Ward Van Allen ☉ Springfield, Mass.; Albany (N. Y.) Medical College, 1891; member of the House of Delegates of the American Medical Association, 1912-1913; member

of the American Roentgen Ray Society, New England Roentgen Ray Society and the Radiological Society of North America; president of the American College of Radiology; on the staffs of the Springfield and Wesson hospitals, Mary Lane Hospital, Ware, and Cooley-Dickinson Hospital, Northampton; aged 69; died, August 2, of coronary thrombosis and cerebral embolism.

Golder Lewis McWhorter ☉ Chicago; Rush Medical College, Chicago, 1913; associate clinical professor of surgery at his alma mater; member of the Western Surgical Association; fellow of the American College of Surgeons; served during the World War; on the staffs of the Presbyterian Hospital, Oak Forest Infirmary and Cook County Hospital; author of numerous surgical papers, especially on the gallbladder and gastrointestinal tract; aged 50; died, October 16, of retroperitoneal sarcoma and uremia.

Frank Clifford Ard, Westfield, N. Y.; University of Maryland School of Medicine, Baltimore, 1887; member of the American Laryngological, Rhinological and Otolological Society; fellow of the American College of Surgeons; formerly on the staffs of the Muhlenberg Hospital, Plainfield, N. J., Somerset Hospital, Somerville, N. J., and the Bonnie Burn Sanatorium, Scotch Plains, N. J.; aged 74; died, August 23, of arteriosclerotic heart disease and aneurysm.

John Dillon Stewart ☉ New York; Medical College of Indiana, Indianapolis, 1905; professor of clinical surgery at the New York Post-Graduate Medical School, Columbia University; member of the American Proctologic Society; fellow of the American College of Surgeons; aged 57; on the staffs of the Bushwick Hospital, Brooklyn, and the New York Post-Graduate Hospital, where he died, August 3, of subacute bacterial endocarditis.

Allan Rupert Cunningham, Halifax, N. S., Canada; Dalhousie University Faculty of Medicine, Halifax, 1904; assistant professor of diseases of the eye at his alma mater; member of the American Academy of Ophthalmology and Oto-Laryngology; fellow of the American College of Surgeons; on the staff of the Victoria General Hospital; aged 50; died, July 3, of pulmonary tuberculosis.

Walter Freeman Taylor ☉ Dallas, Texas; University of Louisville (Ky.) School of Medicine, 1930; an Associate Fellow of the American Medical Association; associate professor of biochemistry and chemical pathology at Baylor University College of Medicine; served during the World War; aged 47; died, August 7, of coronary thrombosis.

Charles A. Hall, Cleveland; Homeopathic Hospital College, Cleveland, 1888; Cleveland College of Physicians and Surgeons, Medical Department of Ohio Wesleyan University, Cleveland, 1899; fellow of the American College of Surgeons; for many years on the staff of St. John's Hospital; aged 74; died, August 19, of tetanus and bronchopneumonia.

George A. Tripp ☉ South Bend, Wash.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1899; fellow of the American College of Surgeons; secretary of the Pacific County Medical Society; formerly county health officer; one of the medical directors of the Pacific General Hospital; aged 66; died, August 11.

Robert Dannelly Schimmelpfennig ☉ Montclair, N. J.; Tulane University of Louisiana School of Medicine, New Orleans, 1908; member of the Radiological Society of North America; served during the World War; on the staff of the Mountainside Hospital; aged 56; died, August 10, in Belmar of coronary occlusion.

Howard Clyde Rockwell ☉ Lansing, Mich.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1912; formerly secretary of the Ingham County Medical Society; editor of the *Bulletin of the Ingham County Medical Society*; aged 51; died in August of carbon monoxide poisoning, self administered.

Edville Gerhardt Abbott, Portland, Maine; Medical School of Maine, Portland, 1898; member of the Maine Medical Association; fellow of the American College of Surgeons; on the staffs of the Maine General Hospital and the Children's Hospital; aged 66; died, August 27, of coronary occlusion.

John Burton Ro Bards, Harrodsburg, Ky.; Hospital College of Medicine, Louisville, 1897; member of the Kentucky State Medical Association; served during the World War; member of the school board; formerly member of the state legislature; aged 68; died, August 11, of angina pectoris.

Owen Wynne Butler ☉ Nicholasville, Ky.; University of the City of New York Medical Department, 1894; member of the Missouri State Medical Association; aged 73; died, August 11, in the Good Samaritan Hospital, Lexington, of carcinoma at the ampulla of Vater and subdiaphragmatic abscess.

Ben Hill Turner, Cleburne, Texas; Louisville (Ky.) Medical College, 1904; member of the State Medical Association of Texas; past president of the Johnson County Medical Society; county health officer; on the staff of the Cleburne Sanitarium; aged 62; died, August 12, of coronary occlusion.

Charles Hewitt Randall, Newark, N. J.; College of Physicians and Surgeons, Medical Department of Columbia College, New York, 1891; member of the Medical Society of New Jersey; aged 73; died, August 3, in the Newark City Hospital of arteriosclerosis and cerebral hemorrhage.

Sylvester Edward Ryan * Springfield, Mass.; Columbia University College of Physicians and Surgeons, New York, 1905; served during the World War; on the staff of the Mercy Hospital; aged 56; died, August 9, at his home in Longmeadow of hypertension and coronary thrombosis.

Homer Allen Walkup * Mount Hope, W. Va.; Medical College of Virginia, Richmond, 1914; past president and secretary of the Fayette County Medical Society; at one time city health officer; aged 49; died, August 19, in the Laird Memorial Hospital, Montgomery, of myocarditis.

Charles Shanks, New Bedford, Mass.; Harvard University Medical School, Boston, 1903; member of the Massachusetts Medical Society; served during the World War; formerly medical inspector in the city schools; aged 59; died, August 2, of carcinoma of the intestine.

Axel Wilhelm Swedenburg * Thief River Falls, Minn.; Chicago College of Medicine and Surgery, 1907; served during the World War; formerly on the staff of the Physicians Hospital; aged 65; died, August 20, of cerebral hemorrhage and arteriosclerosis.

Charles Delbert Snively, Ipava, Ill.; College of Physicians and Surgeons, Keokuk, Iowa, 1897; served during the World War; member of the Illinois State Medical Society; secretary of the Fulton County Medical Society; aged 63; died, August 2, of heart disease.

Harrison Christian Riegel, Keocoughtan, Va.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1905; aged 60; on the staff of the Veterans Administration Facility, where he died, August 5, of heart disease.

Thomas Shirley Venard * Ness City, Kan.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1902; veteran of the Spanish-American and World wars; aged 62; died, August 29, of chronic myocarditis.

William Hervey Albright, Alpha, N. J.; Medico-Chirurgical College of Philadelphia, 1899; for many years member and secretary of the board of education; aged 72; died, August 7, in the Easton (Pa.) Hospital of cerebral hemorrhage.

Edward J. Brennan, Indianapolis; University of Buffalo School of Medicine, 1871; aged 86; honorary member of the staff of St. Vincent's Hospital, where he died, August 2, of chronic myocarditis and arteriosclerosis.

Everette Majette Leake, Norfolk, Va.; University of Maryland School of Medicine, Baltimore, 1926; on the staff of the Leigh Memorial Hospital; aged 37; died, August 8, of hypertension and cerebral hemorrhage.

Frank Marion Fitch * Indianapolis; Medical College of Indiana, Indianapolis, 1904; for many years on the staff of the Methodist Episcopal Hospital; aged 63; died suddenly, August 21, of chronic myocarditis.

Mason Combs, Pineville, Ky.; Hospital College of Medicine, Louisville, 1905; served during the World War; aged 55; died, August 31, in the Veterans' Administration Facility, Lexington, of coronary occlusion.

Ivy W. Moorman, Douglas, Ga.; University of Georgia Medical Department, Augusta, 1897; member of the Medical Association of Georgia; aged 70; died, August 10, of coronary thrombosis and diabetes mellitus.

Carl Schurtz, Streator, Ill.; Marion-Sims College of Medicine, St. Louis, 1900; member of the Illinois State Medical Society; aged 62; died, August 13, in St. Mary's Hospital following a gallbladder operation.

Roy Raymond Miller, Mound City, Mo.; Ensworth Medical College, St. Joseph, 1905; member of the Missouri State Medical Association; aged 55; died, August 6, of nephritis, hypertension and heart disease.

Edward Marquette Harrington, Chicago; Northwestern University Medical School, Chicago, 1924; member of the Illinois State Medical Society; aged 40; died, August 22, in Peoria, of coronary occlusion.

James Eugene Pritchard, Aurora, Ill.; Washington University School of Medicine, St. Louis, 1908; member of the Illinois State Medical Society; aged 52; died, August 6, of amyotrophic lateral sclerosis.

Tharos Harlan, Auburn, W. Va.; George Washington University School of Medicine, Washington, D. C., 1905; at one time served in various capacities with the U. S. Navy; aged 58; died, August 2, of angina pectoris.

William B. Fuqua, Radford, Va.; University College of Medicine, Richmond, 1897; member of the Medical Society of Virginia; for many years city coroner; aged 64; died, August 18, of cerebral hemorrhage.

George W. King, Charlevoix, Mich.; Wisconsin College of Physicians and Surgeons, Milwaukee, 1906; member of the Michigan State Medical Society; aged 70; died, August 22, of uremia following pyelitis.

Alexander Hamilton S. Rouss, Charles Town, W. Va.; University of Pennsylvania Department of Medicine, Philadelphia, 1906; served during the World War; aged 56; died, August 28, of myocarditis.

Claudius Abijah Hayworth, Asheboro, N. C.; University of Maryland School of Medicine, Baltimore, 1913; aged 55; died, August 5, in a hospital at Winston-Salem of cirrhosis of the liver and diabetes mellitus.

Jerome Josephus Stout, Dayton, Ohio; Ohio Medical University, Columbus, 1902; member of the Ohio State Medical Association; aged 61; died, August 25, at the Miami Valley Hospital of heart disease.

Walter Scott Keyting, Salt Lake City; University of Pennsylvania School of Medicine, Philadelphia, 1912; member of the Utah State Medical Association; aged 51; died, August 8, of coronary thrombosis.

Robert Benjamin Porter * Glenwood Springs, Colo.; Denver and Gross College of Medicine, 1906; medical director of a hospital bearing his name; aged 58; died, August 11, of cardiovascular disease.

John Mortimer Crowe * Watertown, N. Y.; College of Physicians and Surgeons, Medical Department of Columbia College, New York, 1887; aged 75; died, August 13, of acute nephritis and uremia.

Clarence Starr Cutter, Cleveland; Cleveland Medical College, 1894; aged 70; on the staff of the Glenville Hospital, where he died, August 19, of influenza, bronchopneumonia and cerebral embolus.

William Simeon Miller, Estelline, Texas; University of Louisville (Ky.) Medical Department, 1881; member of the State Medical Association of Texas; aged 79; died, August 17, of endocarditis.

Franklin T. Poehtler, Minneapolis; University of Minnesota College of Medicine and Surgery, Minneapolis, 1896; aged 66; died, August 3, in the General Hospital of a self-inflicted bullet wound.

Eugene R. Smith, Andalusia, Ala.; Maryland Medical College, Baltimore, 1904; member of the Medical Association of the State of Alabama; aged 59; died, August 25, of cerebral hemorrhage.

William Canfield Dean, Jericho, N. Y.; University of the City of New York Medical Department, 1897; aged 61; died, August 21, in the Nassau Hospital, Mineola, of gastrointestinal hemorrhage.

Robert Lester Allen, Haskell, Okla.; University of Arkansas School of Medicine, Little Rock, 1905; aged 65; died, August 31, of hypertension, arteriosclerosis and cerebral hemorrhage.

Charles Wesley Froedge, Glasgow, Ky.; University of Louisville Medical Department, 1893; member of the Kentucky State Medical Association; aged 72; died, August 7, of coronary thrombosis.

David Nicholas Schaffer, Evanston, Ill.; Loyola University School of Medicine, Chicago, 1916; aged 52; died, August 24, in the Westlake Hospital, Melrose Park, of adenocarcinoma of the rectum.

Walter N. John * Hugo, Okla.; University of Texas School of Medicine, Galveston, 1894; formerly county health officer; aged 67; died, August 15, in the Sanitarium of Paris, Texas, of carcinoma.

Harry Lent Russell, Newark, N. J.; Hahnemann Medical College and Hospital, Chicago, 1901; aged 71; died, August 21, in the Newark Convalescent Hospital of coronary occlusion and empyema.

Charles F. Culver, Howell, Mich.; Jefferson Medical College of Philadelphia, 1900; member of the Michigan State Medical Society; aged 67; died, August 19, of coronary occlusion.

Herbert Benjamin Wren ♂ Shreveport, La.; Memphis (Tenn.) Hospital Medical College, 1900; aged 65; died, August 11, in the Tri-State Hospital of carcinoma of the prostate.

William Jacob Rabenau, Springfield, Mo.; Missouri Medical College, St. Louis, 1885; member of the Missouri State Medical Association; aged 80; died, August 26, of chronic nephritis.

William J. Harrell, Elkhville, Ill.; Memphis (Tenn.) Hospital Medical College, 1883; past president of the high school board of education; aged 78; died, August 21, of cerebral hemorrhage.

Abraham Frank, Philadelphia; Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin, Prussia, 1901; aged 67; died, August 17, in Atlantic City, N. J., of cardiac decompensation.

Albert Henry Parks, Minneapolis; Northwestern University Medical School, Chicago, 1906; member of the Minnesota State Medical Association; aged 58; hanged himself, August 30.

Ollie Thomas Lowery ♂ Tolu, Ky.; University of Louisville Medical Department, 1907; served during the World War; aged 55; was accidentally shot and killed, August 7.

Benjamin Harrison Gibson, Allenhurst, Ga.; University of Maryland School of Medicine, Baltimore, 1909; member of the Medical Association of Georgia; aged 51; died, August 3.

Spero G. Bicasos Vryonis, Bridgeport, Conn.; Georgia College of Eclectic Medicine and Surgery, Atlanta, 1912; aged 54; died, August 9, in Athens, Greece, of heart disease.

Caroline Frances Brooks Woodruff, Independence, Iowa; Boston University School of Medicine, 1884; aged 86; died, August 20, of an injury of the hip received in a fall.

John A. McCulloch ♂ Maryville, Tenn.; University of Tennessee Medical Department, Nashville, 1901; aged 62; died, August 12, in Knoxville, of coronary sclerosis.

Edward Chambers Laird, Morehead City, N. C.; University of Maryland School of Medicine, Baltimore, 1877; aged 83; died, August 21, of uremia and nephritis.

Finley P. Johnson, Hoopeston, Ill.; Rush Medical College, Chicago, 1885; aged 82; died, August 8, in the Lake View Hospital, Danville, of bronchopneumonia.

Gerald Andrew Scully ♂ Silver Spring, Md.; Georgetown University School of Medicine, Washington, D. C., 1927; aged 38; died, August 29, of aplastic anemia.

William Luther Cameron, Lincoln, Neb.; Drake University College of Medicine, Des Moines, Iowa, 1887; aged 83; died, August 14, of Addison's disease.

Frank Harold Boyd, Allendale, S. C.; University of Georgia School of Medicine, Augusta, 1892; aged 68; died, August 9, of pulmonary tuberculosis.

Albert Elmer Derwent, Clinton, Mo.; Rush Medical College, Chicago, 1897; aged 77; died, August 27, in the Research Hospital, Kansas City, of pneumonia.

John Louis Snow, Montgomery, Ala.; Medical College of Alabama, Mobile, 1891; aged 70; died, August 3, of arteriosclerosis and cerebral hemorrhage.

David Cameron Murray, Toronto, Ont., Canada; University of Toronto Faculty of Medicine, 1904; aged 63; died, August 14, in Campbellton, N. B.

Carig Tipton Lewis, McKinney, Texas; Kentucky School of Medicine, Louisville, 1900; aged 78; died, August 7, in the City Hospital of lobar pneumonia.

George T. Williamson, Ellenwood, Ga.; Southern Medical College, Atlanta, 1893; formerly bank president; aged 75; died, August 17, of chronic myocarditis.

John B. Conkling, Cooperstown, N. Y.; Eclectic Medical Institute, Cincinnati, 1883; aged 78; died, July 18, of cerebral hemorrhage and arteriosclerosis.

Charles Augustus Dennett ♂ Sebago, Maine; Medical School of Maine, Portland, 1888; aged 75; died, August 11, in Portland of cerebral thrombosis.

George Archibald Hutcheson, Capron, Ill.; Northwestern University Medical School, Chicago, 1909; aged 53; died, August 4, of injuries received in a fall.

David L. Gaillard, Greenville, Texas; Louisville (Ky.) Medical College, 1877; aged 84; died, August 24, following an operation for thyroid disease.

Joseph Shinglman ♂ Cicero, Ill.; Illinois Medical College, Chicago, 1909; formerly city health officer; aged 58; died, August 7, of angina pectoris.

Clarence Snyder, Arcadia, Ohio; University of the South Medical Department, Sewanee, Tenn., 1894; aged 67; died, August 7, of arteriosclerosis.

Henry Homer Black, London, Ont., Canada; Western University Faculty of Medicine, London, 1906; aged 63; died, August 10, of heart disease.

Adolf George Kaumeyer, Maybee, Mich.; Michigan College of Medicine and Surgery, Detroit, 1897; aged 64; died, August 2, of heart disease.

Albert T. Washburn, Taylorville, Ill.; Chicago Homoeopathic Medical College, 1891; aged 67; died, August 5, in Edinburgh of heart disease.

Fred E. Calkins, Fremont, Neb.; State University of Iowa College of Homeopathic Medicine, Iowa City, 1899; aged 72; died, August 28, of uremia.

M. Hugh Cobb, Thomasville, Ga.; Meharry Medical College, Nashville, Tenn., 1897; aged 69; died, August 28, in Quitman of heart disease.

Dudley W. Lane, Philadelphia; Jefferson Medical College of Philadelphia, 1882; aged 79; died, July 20, of acute dilatation of the heart.

Arthur Frank Kleykamp, St. Louis; Washington University School of Medicine, St. Louis, 1902; aged 58; died, August 26, of pneumonia.

James Scott Cummings, Bronson, Kan.; Cincinnati College of Medicine and Surgery, 1880; aged 86; died, August 26, of myocarditis.

Angus Maybin Ferguson, Deming, N. M.; Medical College of Alabama, Mobile, 1903; aged 61; died, August 5, of heart disease.

William J. C. Casely, Marengo, Ill.; Chicago Medical College, 1885; aged 76; died, August 2, of atrophic cirrhosis of the liver.

Norvin G. Perry Sr., Worthville, Ky.; Miami Medical College, Cincinnati, 1871; aged 92; died, August 21, of cerebral hemorrhage.

Timothy Joseph Cullinane, Andover, Mass. (licensed in Massachusetts in 1906); aged 58; died, August 14, of chronic myocarditis.

George R. Jones, Galena, Md.; Atlantic Medical College, Baltimore, 1907; aged 57; died, August 27, of heart disease and nephritis.

William Warner Wentworth, New York; Albany (N. Y.) Medical College, 1893; aged 69; died, August 16, in St. Vincent's Hospital.

George W. Hous, Dayton, Ohio; Medical College of Ohio, Cincinnati, 1877; aged 89; died, August 7, of heart disease and nephritis.

P. L. Freeland, Proctor, W. Va.; Hospital College of Medicine, Louisville, Ky., 1889; aged 75; died, August 22, of coronary sclerosis.

John W. Snider, Fairland, Ind.; Rush Medical College, Chicago, 1870; aged 93; died, August 6, of pulmonary tuberculosis.

T. Lester Jones ♂ Lansing, N. C. (licensed in North Carolina in 1909); aged 54; died, August 1, of diabetes mellitus.

Frederick James Colling, Toronto, Ont., Canada; University of Toronto Faculty of Medicine, 1901; died, August 13.

Andrew Hyden, Aleester, S. D.; Keokuk (Iowa) Medical College, 1894; aged 75; died, August 21, of pernicious anemia.

Lloyd L. Hall ♂ Youngstown, Ohio; Baltimore Medical College, 1902; aged 62; died, August 1, of coronary occlusion.

Joseph Luther Sheppe, Huntington, W. Va.; Maryland Medical College, Baltimore, 1907; aged 82; died, August 24.

Lloyd M. Bell, Pataskala, Ohio; Toledo Medical College, 1885; aged 79; died, August 16, of cerebral hemorrhage.

Frank S. Peck, Oklahoma City; St. Louis Eclectic Medical College, 1874; aged 97; died, August 14, of senility.

Luther Howard Cartledge, Atlanta, Ga.; Southern Medical College, Atlanta, 1882; aged 82; died in August.

Robert Leighton Island, Toronto, Ont., Canada; Trinity Medical College, Toronto, 1880; died, August 14.

Kansas D. Davis, Chattanooga, Tenn.; Atlanta Medical College, 1881; aged 81; died, August 13.

James Grant McKenzie, Paragould, Ark. (licensed in Arkansas in 1903); died, August 10.

Bureau of Investigation

PRO-KER LABORATORIES, INC.

The Mails Are Closed to a "Hair Replacement" Scheme

The Pro-Ker Laboratories, Inc., was a concern that sold through the mails a "treatment" called "Pro-Ker Hair Milk" which, it was claimed, would prevent premature baldness and replace falling hair. The business was incorporated in New York in 1932. In March of this year the concern was called on to show cause why a fraud order should not be issued against it and its officers, as such. On April 4 the president of the concern, Charles G. Nessler, accompanied by an attorney, appeared in Washington and a hearing was held. On June 24, after going over all the evidence in the case and also considering a brief submitted by the concern's attorney, the Acting Solicitor for the Post Office Department, the Hon. W. E. Kelly, recommended to the Postmaster General that a fraud order be issued. The order was issued on June 30, 1938.

As long ago as August 1936 the Federal Trade Commission issued a complaint against the Pro-Ker Laboratories, Inc.,

charging that the advertisements which represented Pro-Ker as a competent treatment for baldness were false. The commission, however, did not issue an order for the company to cease its false statements until Sept. 9, 1938—more than two months after the Post Office officials had closed the mails to it.

The Pro-Ker Laboratories, Inc., caught its suckers with the usual bait: newspaper advertisements. The company was incorporated by the father of the president of the concern, Charles Nessler senior, who, it has been claimed, was the inventor of the "permanent wave." In 1927 Nessler senior published a book entitled "The Story of Hair." The reviewers seem to have given it a "good press," judg-

Let's face the facts about Hair and Hair Replacement

Charles Nessler, founder of Pro-Ker Laboratories, Inc., inventor of permanent waves.

It's time we called a halt to the endless flow of useless creams, lotions and ointments, offered a glibble public to arrest baldness. Let's name every product, every system, bid to stand the light of science—meet the test of performance.

To me the question of baldness is a serious matter—the subject of over 40 years' research. I have studied it on the heads of thousands of men and women, in all climates, under all conditions.

How Hair Should Grow in Continuity

I have seen baldness come on some heads as early as eight months old, and I learned why! That was the first step, the major step, in solving the problem.

Each year I came nearer my goal. Finally I perfected the Pro-Ker Treatment. Pro-Ker did the job. I saw it work on hundreds of heads. It helped arrest baldness by encouraging normal hair replacement.

Money-Back Guarantee

Send for free copy of Nessler's valuable book "The End of the Bald Era." Write Pro-Ker Laboratories, Dept. D1, 400 Madison Ave., New York.

PRO-KER
THE SCIENTIFIC HAIR TREATMENT

ing from the excerpts published by Nessler in promoting Pro-Ker. Such favorable reviews will not surprise those familiar with the close community of interest between the book review departments and the advertising offices of some newspapers.

In its advertisements the Pro-Ker Laboratories, Inc., urged the public—at least that part of the public which feared loss of hair—to send for its free booklet "The End of the Bald Era." Even such a careful and conservative paper as the *New York Times Magazine* carried a full page advertisement of the booklet in its issue of Nov. 13, 1932. Those who sent for the booklet were told that the secret of "hair replacement" lay in the use of Pro-Ker, which the company described as "Hair Milk," together with the following of certain directions regarding the care of the scalp.

Pro-Ker was analyzed for the Post Office Department by the chemists of the Food and Drug Administration of the Department of Agriculture. They reported:

"The product is a milky liquid with a lavender-like odor and a soapy taste. It consists of a small amount of sodium sulfate [Glauber's Salt, sometimes called Horse Salt, because used by veterinarians] and a small amount of fatty oil emulsified in water by means of a soap—a sulfonated oil soap is indicated. A small amount of formaldehyde is present and also traces of volatile oils, among which oil of lavender is indicated."

Two physicians testified on behalf of the government at the hearing at Washington, but the Nessler concern did not present any witnesses at all. In the brief submitted by the Nessler attorney after the hearing it was contended that the action of the Post Office was obnoxious to the Fifth Amendment to the Constitution of the United States and constituted a deprivation of property without due process of law! Such a contention was wholly without foundation, as the postal fraud order laws have been held constitutional repeatedly by the United States Supreme Court. The brief also charged that the action of the postal authorities was an attack "aimed at the theories and opinions of Charles Nessler." Acting Solicitor Kelly, in his memorandum to the Postmaster General, pointedly replied that Nessler's counsel had entirely missed the point; that the proceedings in the case were directed not at the theories and opinions of Nessler but against the false and fraudulent pretenses, representations and promises contained in the written and printed matter that the Pro-Ker Laboratories, Inc., sent through the United States mails. Mr. Kelly further emphasized that a person who has made false and fraudulent claims "as to the curative properties of a treatment which he is selling cannot, when pursued by justice, take refuge in the statement that he was expressing his opinion."

The memorandum to the Postmaster General also brings out the fact that purchasers of Pro-Ker bought the product on the representation, among others, that it would retain on the scalp of the user at least the same amount of hair which existed when the treatment was started or, alternatively, would reestablish the amount of hair within seven months and arrest further hair loss. The facts were, said Mr. Kelly, that Pro-Ker did not and could not achieve such a result.

As previously stated, the fraud order against the Pro-Ker Laboratories, Inc., and its officers and agents as such, was issued June 30, 1938.

TUBRON

The Fraudulent Consumption Cure of H. G. Haring

Henry G. Haring, a druggist who conducted a small drug store in Philadelphia, sold through the mails a preparation called "Tubron" or "Tubron (Haring)" as a treatment for the cure of tuberculosis. Haring obtained his victims by advertising in certain newspapers that were not above sharing the profits to be made by swindling consumptives.

When Haring was called on by the Post Office officials to show cause why a fraud order should not be issued against him, a written answer was submitted by an attorney who indicated that if the enterprise were found to be an improper one his client would discontinue it. The postal authorities thereupon furnished the respondent with a form of affidavit providing for the discontinuance of the enterprise. But Haring refused to execute the affidavit!

According to the evidence in the case, Haring claimed that "after 30 years of study, research, experiment, application and observation" he had perfected a remedy for tuberculosis. He declared that, while good food, rest and fresh air were "good adjuncts" to the treatment of tuberculosis, "Tubron" was "the essential treatment." When analyzed by government chemists, Tubron was found to be essentially an emulsion of cod liver oil and hypophosphites with small amounts of strychnine, oil of wintergreen, alcohol and water. The amount of cod liver oil found was much too small for any practical purpose and the mixture might in many instances prove harmful because it would upset the digestion.

In his memorandum to the Postmaster General, recommending the issuance of a fraud order, the acting solicitor for the Post Office Department, the Hon. W. E. Kelly, brought out the fact that Haring's "patent medicine" was worthless and was not, as claimed, a "rapid and permanent cure" for tuberculosis. It was declared too that Haring's scheme was a fraudulent one and urged that the mails be closed to Haring's Pharmacy, H. G. Haring and the West Philadelphia Tuberculosis Dispensary. On July 1, 1938, the fraud order was issued and the mails closed to these names, as recommended.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

TREATMENT OF DOG BITE

To the Editor:—I recently noted the correspondence in THE JOURNAL relative to the treatment of dog bite with fuming nitric acid. Will you please explain the rationale of this treatment? Is there any record of rabies ever having been prevented with this treatment following the bite of a proved rabid dog without the use of the Pasteur treatment? Is it not true that the only treatment of any avail whatever is the Pasteur treatment or a modification of it? If this is true, why should the patient be subjected to the discomfort and probable scarring which follows the treatment with fuming nitric acid? To my mind, the only treatment necessary for dog bite is the usual treatment given in any other wound which might be infected, plus the Pasteur treatment if the dog is rabid or if there is a suspicion that the dog is rabid. It seems to me that there is a lot of unnecessary disturbance about the treatment of the usual dog bite.

MARVIN D. SHIE, M.D., Lakewood, Ohio.

ANSWER.—There is certainly a difference of opinion on this subject and there is some weight to the view expressed. Some believe that there is no logical basis for the assumption that the use of fuming nitric acid prevents the development of rabies. Others, as previously mentioned, maintain that nitric acid should be used if the dog is mad, has suggestive symptoms or is unidentified. Experiments with guinea pigs seem to show that rabies can be prevented in a large number by means of fuming nitric acid. In the light of present available evidence it does not seem that one should be criticized for the use of nitric acid, although in a few years the entire method of treatment may be changed.

BENZOYL PEROXIDE IN FLOUR

To the Editor:—Please give me some information concerning the toxicity of benzoyl peroxide, sold under the trade name of Novadel and used as a bleaching agent in the preparation of flour. I understand that this substance is used in the proportion of 1 ounce to 200 pounds of flour. What harmful effects, if any, might be expected from ingestion of flour in which this substance was used in the proportion of 50 ounces to 200 pounds?

M.D., Oklahoma.

ANSWER.—The usual person consumes less than 1 pound of flour a day, but an exceptionally active man, consuming in the neighborhood of from 4,000 to 5,000 calories daily, may utilize as much as 2 pounds in the form of bread, pastry and sauces. Under these extreme conditions, such a person might consume one-half ounce of the benzoyl peroxide if flours containing the peroxide in the proportions of 50 ounces to 200 pounds were ingested. In toxicology, this substance is chiefly associated with bakers as one of the sources, but perhaps not the foremost source, of "bakers' itch." The substance enjoyed some use as an external disinfectant and skin anesthetic but occupies a position today of little recognition. Little is known about its action after ingestion in large quantities, but there are reasons to believe that it may cause gastrointestinal irritation and hamper digestive processes through local anesthetic action. In the intestinal tract it is believed to decompose in part to benzoic acid and/or benzaldehyde.

Paul D. Lamson (THE JOURNAL, Aug. 30, 1930, p. 663) states that benzoyl peroxide "is extremely nonirritating, watery solutions causing no irritation when dropped in the eye, and even the pure crystalline substance causing no irritation or disturbance of any kind when placed in the peritoneal cavity. It is also nontoxic when taken by mouth, being reduced to benzoic acid and excreted as hippuric acid. Saturated water solutions have been given intravenously without toxic effects."

Note is made of the fire and explosion hazard related to this substance. Reports of accidents with benzoyl peroxide are on record, and caution should be exercised in handling it.

It should be further noted that the proportion of 50 ounces of benzoyl peroxide to 200 pounds of flour, or one part of benzoyl peroxide to sixty-four parts of flour, appears excessive. The Council on Foods has accepted a number of brands of flour which are artificially bleached with nitrogen chloride and a mixture of calcium phosphate and benzoyl peroxide in the proportions of one-tenth ounce of nitrogen chloride to 196 pounds of flour and one part of the mixture of calcium phos-

phate and benzoyl peroxide to 50,000 parts of flour. Two pounds of such flour would contain a maximum of 0.02 Gm. of benzoyl peroxide. Available evidence (Sollmann, Torald: A Manual of Pharmacology, ed. 5, Philadelphia, W. B. Saunders Company, 1936, p. 602) indicates that healthy persons may safely consume as much as 0.5 Gm. of benzoate a day in concentration of 0.1 per cent if these foods are not otherwise spoiled or unhealthful but that patients with gastrointestinal diseases would do better to avoid it. It is quite conceivable that irritant actions which would be too feeble to influence normal organs might become deleterious to these organs, especially the gastrointestinal tract or kidneys, if these are already diseased or if the general resistance is lowered. The Council on Foods requires that all accepted flours which are artificially bleached carry the word "Bleached" in a conspicuous position on the package label and publishes with each announcement of acceptance the amount and kind of bleaching agent used.

CONTACT DERMATITIS FROM RHODIUM OR NICKEL

To the Editor:—A woman acquired a local contact dermatitis from wearing a bracelet for several hours. The bracelet consisted of a basic white metal on which had been successively plated nickel and rhodium. Could the rhodium, which was the superficial metal, have been the cause of the dermatitis? If so, what is the relationship to skin hypersensitiveness? What are the other possibilities?

M.D., New York.

ANSWER.—The diagnosis of contact dermatitis in this case is obvious. The only question is as to the cause, whether nickel or rhodium or perhaps some other metal. Rhodium is a metal in the platinum group and is closely allied to iridium. It is used in the manufacture of liquid gold and is also used as an outer coat in some silverware to prevent tarnish. Some of the salts of rhodium are pink, and some cosmetics may possibly contain one of these salts, although this has not been proved.

A search of the literature revealed no reports of dermatitis due to rhodium. On the other hand there have been many cases of dermatitis from contact to nickel. Weber (External Causes of Dermatitis, Arch. Dermat. & Syph. 35:129 [Jan.] 1937) gives a list of external irritants and a review of the literature on contact dermatitis. Foster and Ball (Sources of Nickel Eczema, ibid. 31:461 [April] 1935) review the literature on nickel dermatitis and report several cases. They consider nickel capable of causing a definite sensitivity; they state that the incubation period is from eight to thirty days between the first contact with nickel and the development of the dermatitis.

To discover the cause in this patient, patch tests with nickel and rhodium should be made on clear skin, e. g. the back. Foster and Ball give the details. The test is simple.

Contact dermatitis is a form of hypersensitiveness in which the skin alone suffers. Almost every one can acquire contact dermatitis provided the contact is sufficiently close and sufficiently prolonged. This has been proved in cases of primrose sensitivity, which is another variety of contact dermatitis. Patch tests are usually positive and ordinary cutaneous and intracutaneous tests are negative. There is no family history of allergy and passive transfer tests are negative. In one of the "nickel" cases of Foster and Ball the passive transfer test was reported as positive.

WAX FOR REMOVAL OF HAIR—X-RAYS AS DEPILATORY

To the Editor:—1. Please furnish a prescription for preparing a wax which may be applied to the body and by its removal extract excessive hair. How is it used? How often would a heavy growth of black hair have to be removed from the legs with wax? Is there a better method of meeting the situation than by removal with wax? 2. Is there a safe method of removing an excessive growth of hair from the eyebrows and forehead by means of x-ray treatments?

M.D., California.

ANSWER.—1. The simplest formula for epilating wax is that given by William Allen Pusey (Recipe for Epilating Wax, THE JOURNAL, Aug. 28, 1926, p. 663): beeswax 1 part by weight, finely powdered rosin 4 parts by weight. Melt the beeswax over a slow fire and pour in the rosin, stirring gently for a few minutes until all is melted. Mold on a greased dish, marking the cooling cake in rectangles, or pour into cylinders of waxed or greased paper with the bottom folded shut.

There are a number of more complicated formulas. There is no reason to think that they are any better than the simplest.

To apply, heat one of the cakes on the end of a stick over a flame until soft. When cooled to a bearable temperature, rub it on the hair to be removed, rubbing in the direction of the hair, until the wax is about an eighth of an inch thick, pressing it down well on the hair. When cool, loosen the end next the ends of the hair and pull off the whole mass in the direction

opposite to the growth of hair. If well done only a few hairs will remain and these can be removed with tweezers. Pusey states that the procedure is only slightly uncomfortable.

The advantage of this method lies in its applicability to a generous growth of fine hair, a difficult, tedious and expensive task for electrolysis. The result is much more lasting than that from shaving or chemical epilation. It is impossible to say just how quickly the hair will return after this procedure. It depends on the individual and the part of the skin involved; but another treatment should not be necessary for at least two months, according to Giovannini, quoted by Jackson and McMurtry (*Diseases of the Hair*, Philadelphia, Lea & Febiger, 1912, p. 42).

The other practical methods of hair removal are by electrolysis, shaving and chemical depilatories, the latter of which must be repeated frequently, and grinding down the hair by rubbing with pumice stone in powder or cake form. The latter has its advocates, who claim that continued use of it reduces the hair growth. The method is tedious and it requires some experience to acquire the proper technic. If the hair is coarse, it should be cut short before beginning and it is claimed that lathering the skin makes for success. After the first grind, which may take a half hour to remove the hair completely, it is claimed that a few minutes rubbing each day will keep down the growth and that this can be done without serious skin irritation.

2. An emphatic negative must be returned. Any strength of roentgen rays sufficient to cause atrophy of the hair roots is sure to result in visible atrophy of the skin sooner or later, often with disfiguring telangiectasis. This may not appear for years after the original injury.

RHEUMATOID ARTHRITIS OF SPINE?

To the Editor:—A college graduate, aged 21, weighing 154 pounds (70 Kg.), complains of pains in the adductor muscles and knees and in the lumbosacral region, and of inability to lie quietly for more than three or four hours because of pain. He has had scarlet fever, measles, pertussis and bronchitis during childhood, all of which he recovered from with no complications. In 1933 he had Vincent's angina, in 1934 gonorrhea, for which he has taken treatments regularly for two years, and repeated prostatic smears which have been examined in reliable laboratories and have not shown the presence of gonococci infection. In 1936 while at college he was hospitalized for influenza. About four months ago he began to complain of pains in his knees, adductor muscles of his legs and in his back, which have been continuous since. There has not been any swelling or redness of the knees or of the involved muscles. The pain bothers him severely after lying in bed about three or four hours and he awakens at about 4 in the morning with severe backaches, which are relieved by moving about. These backaches are worse if he has exercised strenuously the previous day but at the time of exercise he does not feel worse. The pain in the adductor muscles of the legs radiates into the scrotum and these muscles are also painful on coughing. There is no increase in pain during sexual relations. Examination showed a white blood count of 13,000, temperature of 99.2 F. and a pulse rate of 96. The blood pressure is 120 systolic, 80 diastolic. The urine is negative for pus, albumin, sugar and blood cells; the sedimentation rate is within the normal range after one and three hours. The tonsils and teeth show no signs of infection. There are no glandular enlargements. Heart and lung examinations are negative; the abdomen is normal. The prostate was normal to palpation and the secretion contains only a few pus cells. The involved regions of the back, legs, scrotum and knees show no evidence of inflammation or edema and are not tender. While at school the patient was told by one doctor that it was not his previous gonorrhea causing his trouble and advised him to have his tonsils removed. Another told him that since his tonsils showed no infection this would be illogical. I agree with this. His condition was diagnosed as neuritis by the second doctor, who treated him with diathermy, a vitamin B compound, rest and the use of a hard, flat bed. He has now returned home for the summer and during the last three weeks has been getting worse. It appears that the man has an infection but I am at a loss to say where. I have also done an agglutination test for Malta fever, which was negative.

M.D., South Dakota.

ANSWER:—It is impossible to make an absolute diagnosis from the data presented. From the information at hand, one should be suspicious of a beginning rheumatoid arthritis involving the spine (Marie-Strümpell type of spondylitis). This diagnosis would adequately explain the low grade fever, leukocytosis, all the symptoms, and the otherwise negative physical examination. X-ray examination of the sacro-iliac joints may reveal bilateral sacro-iliac arthritis. If this is found, the suspicion will be corroborated. One occasionally sees a case of rheumatoid arthritis in the early stages with a normal sedimentation rate. In this particular case a sedimentation rate done by the Rourke-Ernstene method might reveal an abnormal rate. A differential blood count might show a shift to the left. It is improbable that the previous gonorrheal infection has any part in the present illness, nor is it likely that the removal of the tonsils would materially benefit the patient.

If he has a beginning Marie-Strümpell spondylitis, physical examination might reveal limited chest expansion, pain at times

on deep breathing, spasm of the psoas muscles or the para-vertebral muscles, tenderness over either sacro-iliac joint and limited straight leg raising. If the fever and leukocytosis do not persist, one should examine the patient for other causes of backache, such as a ruptured intervertebral disk, lumbosacral strain, postural strain, cord tumor and the like. A complete neurologic examination and detailed examination of the skeletal system should help to make a diagnosis.

If subsequent studies reveal that the patient is suffering from rheumatoid arthritis of the spine, the treatment indicated would be adequate bed rest, a high vitamin, high caloric diet, hot fomentations to the back, control of pain, sleeping on a firm bed, exercises, vitamin concentrates if indicated and a sacro-iliac belt for support if needed.

COMPOSITION OF PATHOLOGIC CALCIFICATION

To the Editor:—Can you tell me the chemical composition of the deposits found in calcified subdeltoid bursitis? I have not been able to find any chemical analysis of this material in any of the articles to which I have had access and would appreciate knowing in just what form this calcium is deposited.

M. E. GOODRICH, M.D., Toledo, Ohio.

ANSWER:—The composition of deposits of pathologic calcification has been studied by MacCordick, Wells and Codman.

H. Gideon Wells (Chemical Pathology, ed. 5, Philadelphia, W. B. Saunders Company, 1925, p. 487) concluded that the chemical composition of deposits in the various types of pathologic calcification was essentially the same as that of bone. Dr. A. Baird Hastings made chemical analyses of the deposits found in calcification of the supraspinatus tendon and subdeltoid bursae and concluded that the composition was essentially the same as that of bone ash. (This work has not been published.)

E. A. Codman (The Shoulder, Boston, Thomas Todd Company, 1934, p. 79) has published the most complete studies of the composition of these deposits. The chemical analyses were made by Dr. J. L. Stoddard, who found that deposits of the inorganic matter of the dried unashed specimen contained 55.8 per cent of calcium phosphate and 42.2 per cent of calcium oxalate. There was 14 per cent of the ash that could not be accounted for by figuring all the phosphate as calcium phosphate and the remaining calcium as carbonate. What this 14 per cent consisted of was not definitely established.

NICOTINE POISONING AND SPRAYING HAZARDS

To the Editor:—What is the health hazard arising in an unmasked person from spraying the following solutions in a greenhouse? The sprayer is exposed for periods of from eight to ten hours daily and no protective measures are employed. The greenhouse contains principally flowers with a high humidity and temperature present. 1. Aqueous solution of 40 per cent nicotine. 2. "Selocide," a commercial product containing 8 per cent potassium ammonium sulfide and seleno sulfide. Any information you can give me on this subject will be appreciated.

R. D. HOWELL, M.D., Indianapolis.

ANSWER:—While various greenhouse plants may lead to dermatoses from direct irritation or as a result of sensitization, and while selenium compounds, as mentioned in the query, and other insecticides may possess some toxic properties, nicotine must be regarded as highly and practically dangerous. Toxicologic literature contains many references to fatalities and to severe poisoning connected with exposure to insecticides containing nicotine. A typical occurrence, appearing in the literature is here excerpted: A girl, employed in the manufacture of insecticides, spilled a few cubic centimeters of a 95 per cent solution of nicotine (probably in the form of sulfate) on one sleeve. Promptly she washed and dried her arm, wiped it on under-sleeve and changed her overalls. Twenty minutes later she collapsed and became pallid and cold, and the pulse was not perceptible. Nicotine was established as present in the vomitus. This patient recovered. This article (*Brit. M. J.* 1:246 [Feb. 11] 1933) carries the statement "Clearly nicotine is a powerful poison when applied to the skin, from which it should be removed by washing with cold water instead of hot, which by flushing the skin increases the rate of absorption." This statement may be supplemented by noting that nicotine poisoning may be induced following either inhalation or ingestion. The lowest grade of nicotine poisoning may be accompanied by dizziness, headache, nausea and vomiting. A slightly severer state in addition may include clammy sweating, visual disturbances, profuse ptialism, diarrhea and collapse. When nicotine is ingested, a sensation of burning may exist in the mouth, gullet and stomach. In severe poisoning, when death does not take place in a few seconds or minutes, mental confusion may appear, together with muscular weakness, restlessness, quick and labored respiration, feeble and irregular heart beat, convulsions and

muscular twitclings. In view of the extensive and often careless use of nicotine insecticides, it appears likely that some degree of toleranc may develop, as in the case of tobacco smokers.

The possibility of sclenium poisoning exists, but the nature of selenium poisoning and the conditions under which it arises are not well known. More information may be found in "Studies on the State of Selenium in the Organism," by M. I. Smith, B. B. Westfall and E. F. Stohlman (*Pub. Health Rep.* 53:1199 [July 5] 1938). It is to be noted that nicotine readily harms rubber, so that natural rubber gloves or gauntlets are somewhat unpractical, but some types of synthetic rubber are more resistant to nicotine action. In the presence of a definite nicotine exposure, as implied in the query, other mentioned exposures, as high humidity and temperature, may be ignored as relatively unimportant.

NEUROCIRCULATORY ASTHENIA

To the Editor:—Physical examination of a man aged 43 reveals the following: height, 5 feet 6½ inches (168 cm.); weight, 165 pounds (75 Kg.); pulse rate, 94 (next day 114), usually from 90 to 100; respiratory rate, 22; temperature, 98.6 F.; blood pressure, 100 systolic, 80 diastolic (always around 100); hemoglobin, 74 per cent; white cells, 11,900; red cells, 5,150,000; urine, normal; basal metabolism, plus five per cent; Mantoux test, negative; Wassermann reaction, negative; eye-grounds, normal. While blood was being drawn for a Wassermann test he had a distinct convulsion of some sort. Convulsive movements of the arms and legs occurred, the eyes rolled back and he lost consciousness for two or three minutes. Immediately after this seizure his pulse was normal for a short time; within a period of ten minutes it dropped from 100 to 72 and remained that way until he left my office a short time afterward. He is the picture of health. He came to me because of terrible attacks of depression. He has these attacks without any cause whatever and they have lasted several weeks at a time. Instead of going to his office he remains around his home and is not fit to do any work. He is secretary and treasurer of a corporation, a position which requires much book-keeping. He is in good circumstances financially. He tells me that he has nothing to worry about at all but that he gets these attacks just the same. X-ray examination of the chest gives negative results. The low blood pressure and constantly rapid heart make me think of Addison's disease but it is not a clear picture of anything that I know of. What can I do for him?

M.D., Indiana.

ANSWER.—The condition which seems most probable is an "autonomic imbalance" or "neurocirculatory asthenia." These terms are really a cloak for ignorance of the actual underlying cause for a clinical syndrome. It is assumed to be some sort of maladjustment between the sympathetic and parasympathetic systems. It is associated with tachycardia, easy fatigue, low blood pressure, syncopal attacks and a general feeling of inadequacy leading to mental depression. It is assumed that the convulsive seizure was a syncopal attack. The one important requirement for diagnosis is that all organic pathologic changes be ruled out. It would not appear that a moderately low blood pressure makes an adequate basis for a diagnosis of Addison's disease.

One must also consider as possibilities a neurosis or a psychosis. An anxiety neurosis or a mild depressive psychosis will present a picture resembling this one. The differential diagnosis of these conditions may be found in any standard textbook on neurology and psychiatry.

The treatment of a neurosis or a psychosis is a highly specialized problem. The treatment of neurocirculatory asthenia is one of intelligent management and encouragement and the avoidance of drugs. Any further suggestions for treatment must be based on a more accurate diagnosis.

CHORDOTOMY FOR SCIATIC NEURALGIA

To the Editor:—A chordotomy has been proposed for a patient with severe and protracted sciatic neuralgia presumably due to osteoarthritis of the spine. Can you give me any information as to the dangers and permanent value of such an operation in the hands of a skilful neurosurgeon? What about the operation of rhizotomy of the posterior nerve roots?

A. T. BLACHLY, M.D., Portland, Ore.

ANSWER.—Either operation suggested appears drastic, but it is assumed that the case is one of unusual severity and long duration and that both sides are affected. Section of the posterior roots is of such uncertain value that it may be dismissed. Bilateral chordotomy in the thoracic region is reasonably certain to give great relief. However, even the most experienced and dexterous neurosurgeon may cut too much, causing some paralysis, or too little, in which case little or no relief is secured and the operation would have to be repeated to be of benefit. However, if all usual methods of treatment have failed chordotomy is the last resort, but the risks should be explained to the patient.

DIAGNOSIS OF SYPHILIS?

To the Editor:—A white woman aged 33 reports that in 1927 a Wassermann test showed a strongly positive reaction. A second Wassermann test was then taken and reported negative. She was told to disregard the first report and received no treatment. About a year later she missed her menstrual period and consulted an obstetrician, who told her she was pregnant. A Wassermann test taken at this time was returned four plus. She received one injection of neosarsphenamine, and another Wassermann test taken about a week after the first was negative. She received no further treatment, but several Wassermann tests taken during her pregnancy were all negative. She delivered a normal full term baby whose Wassermann reaction was negative. Her husband's Wassermann test, taken shortly after hers was returned positive, was negative. She has remained fairly well since the baby was born but has had three spontaneous abortions, all within the first three months of pregnancy. One year ago she had a hemorrhoidectomy because of bright red blood in the stools, pain on defecation and a feeling of fullness in the rectum and of aching in her back and hips. Following the hemorrhoidectomy the rectum was sore for three or four months and the bleeding has continued until the present time. She says that her rectal condition has not been altered in the least by her operation. At the present time she feels nervous and is easily excited and irritated, in addition to her rectal complaint of bleeding, fullness and discomfort on bowel movement, and aching in the hips and back. Her only past illness was diagnosed as scarlet fever at the age of 20. She was not acutely ill and does not remember having peeled at all. There has never been sexual intercourse with any one except her husband. Physical examination at present is negative except for a presystolic mitral murmur, stellate laceration of the cervix, many tags about the rectum and moderately sized internal hemorrhoids. X-ray examination of the chest reveals normal heart and lungs; the blood count and urinalysis are normal. Kolmer's Wassermann reaction was 4 plus in three tubes, twenty-four hours later 2 plus, 2 plus and 1 plus, and twenty-four hours later was reported negative by two competent laboratories. Her spinal fluid was entirely normal. I shall appreciate discussion of the status of this patient.

M.D., Texas.

ANSWER.—It is difficult to say whether this patient has syphilis or not. Much depends on who did the Wassermann test and the type of reaction. It is known that there are such things as false positive Wassermann reactions. At the recent meeting of the American Medical Association in San Francisco there was considerable discussion in the Section on Dermatology and Syphilology on certain cases that have been carefully studied by syphilologists and the blood checked in many different first class laboratories with confusing reports. Another Wassermann test should be taken on the baby, for it is known that a child may have a negative Wassermann reaction at birth and later the serologic reaction may change. The patient's rectal difficulty is apparently from hemorrhoids and can in no way be attributed to syphilis. Moreover, there may be some other explanation for the three spontaneous abortions, for this does not necessarily mean syphilis. As the patient's physical examination is negative, her spinal fluid is entirely normal and she still has what one might term a controversial serologic report on her blood, one would be inclined to recommend no treatment for syphilis. It would probably be well, however, to examine her carefully each year. It might even be advisable to have consultation with a competent internist or syphilologist.

INTERMITTENT HYDRARTHROSIS

To the Editor:—A white man aged 76, with mild diabetes, has recurring simple nontraumatic hydrarthrosis of the left knee joint of about one year's duration. During the year the knee has been aspirated about six times. Culture of the fluid was negative. Twice the knee was immobilized with a cast for about ten days and then treated with diathermy and strapping. The patient has little pain and enjoys good health. He had a prostatectomy about six years ago and the urine is still cloudy. Can you suggest any other treatment, such as injection of air or other medication? Please describe technic.

M.D., New York.

ANSWER.—Two types of intermittent hydrarthrosis are recognized: the first and rarer type is "true intermittent hydrarthrosis," which usually involves one or both knees in recurring attacks remarkable for their regularity, attacks generally coming every ten to fifteen days and usually lasting from two to six days. The second type, "symptomatic intermittent hydrarthrosis," is commoner and represents the early stage of chronic synovitis or of atrophic arthritis which has not yet become generalized but of which, for a while, the symptoms are confined intermittently to one joint, later becoming chronic and polyarticular. If, after one year, this patient presents no evidence of polyarticular involvement and if the erythrocyte sedimentation rate, nonfilamented cell count and erythrocyte count are normal, he may have the first type. To distinguish the two conditions more accurately and promptly, further studies on the comparative cytology and chemistry of synovial fluid are needed. In true intermittent hydrarthrosis the total synovial fluid cell count is generally low (from 400 to 7,000 cells per

cubic millimeter); in atrophic arthritis it is generally considerably higher (from 5,000 to 60,000 cells per cubic millimeter).

The cause of true intermittent hydrarthrosis is unknown. Because the effusions appear rapidly and periodically and disappear without leaving a symptomatic residue, the disease is thought by some to be due to angioneurosis; hence the allergic hypothesis has been advanced. It remains unproved, however. Endocrine disturbance or infection is believed responsible by others. Several cases of intermittent hydrarthrosis associated with undulant fever have been reported (Baker 1928, 1929; Simmons 1935; Sharpe 1936).

Many forms of treatment have been advocated: removal of foci of infection, desensitization by injections of peptone, intravenous injections of triple typhoid vaccine, arsenic, rest, physical therapy, bandages, splints. Ergotamine tartrate (gynergen) was considered of value by Weismann-Nutter (1929). Sometimes the cycles are interrupted temporarily or permanently after the use of one or more of these various measures; in other cases the cycles persist. The hydrops often ceases spontaneously after some months or years. When it seriously handicaps the patient's health or earning power, synovectomy may be indicated (Porter and Lonergan 1932; Krida 1933).

CORD BLADDER AND IMPOTENCE AFTER DISSEMINATED MYELITIS

To the Editor:—A man aged 21 reports that five years ago he had what was diagnosed as acute disseminated myelitis. He was paralyzed from the nipples down but recovered by March 1934. All muscular reactions are normal as well as touch sensation, but he is having trouble with poor bladder control and constipation is extreme. It is impossible for him to have an erection and he has no natural desire for intercourse. As he wants to get married, he would like to know if there is any possibility of improvement along this line.

M.D., Illinois.

ANSWER:—One would expect to find on a sensory examination some disturbance in the sacral region, i. e. saddle anesthesia. Disturbances in urination, defecation and erection indicate a lesion of sacral levels 2, 3, 4 and 5, which is probably a residue of the disseminated myelitis. Cystoscopic examination would probably confirm the diagnosis of cord bladder.

The prognosis depends on the extent of the lesion and whether a normal libido was present and intercourse was possible before the attack. Cases have been described in which erection and intercourse were perfectly possible in extensive lesions of the sacral cord. This is probably due to a cerebral (psychic) mechanism, although bladder and rectal disturbances were still present.

One should try drugs such as strychnine to stimulate any nerves present (1 mg. four times a day). Ergotamine tartrate (gynergen) has been used in tabetic bladders with fair results and may be of some value here. As a last resort some of the androgens should be injected parenterally to see whether some sexual desire could be initiated.

The prognosis at its best is not too favorable but these measures should be tried.

ALLERGY TO CHLORINE

To the Editor:—A youth aged 17 apparently has an allergy to chlorine in bath water, as he breaks out in large red welts during or immediately after a bath. During two years in Virginia, where the water supply is artesian and not chlorinated, this did not occur, but on his return to Chicago it is again manifest. Every type of soap, and no soap, have been tried, but the result is the same. Can you suggest a remedy? His older brother, aged 32, is affected much the same way but less severely. While driving across the Appalachian Mountains five years ago, the same boy complained of pain in his ears on descending from an altitude of 3,000 feet. This sensitiveness has continued through several similar trips and now he feels it when descending in an elevator. Is there any remedy?

M.D., Illinois.

ANSWER:—Allergy to chlorine, while not definitely accepted, has been reported. Duke (*J. Allergy* 3:495 [July] 1932) had a patient, a physician, who acquired coryza, cough and asthma from the use of Dakin's solution, and to the chlorine gas which escaped from diluted solution of sodium hypochlorite. Chlorinated water caused wheals in this patient. Passive transfer of this hypersensitivity to chlorine was not successful. Duke believes that this type of allergy is similar to that found in physical allergy.

Watson and Kibler (*ibid.* 5:197 [Jan.] 1934) reported a case in which chlorine in drinking water was apparently the cause of asthma and colitis. The patient became worse when drinking chlorinated water and was entirely relieved on changing to distilled water. In the discussion which followed the presentation of this paper, Eyermann stated that he had relieved two patients of intractable urticaria by the use of distilled water. These patients had failed to respond to ordinary elimination

diets. Milton Cohen discussed the case of a chemist who had coryza from the inhalation of platinum chloride.

Dutton (*ibid.* 6:477 [July] 1935) reported a case in which severe eczema resulted from the drinking of ordinary tap water; when distilled water was substituted on numerous occasions, the eczema cleared up quickly each time. The author concluded that some allergen or other substance in the drinking water was the etiologic factor but did not specify what this substance was.

From these reports it seems evident that the patient under consideration must avoid contact with chlorinated water. Apparently contact with the water is sufficient. If there is a possibility that drinking such water causes the urticaria, distilled water should be substituted.

The simplest remedy for the pain in the ears on descending from high altitudes is to stuff cotton in the ears.

DERMATITIS FROM BATHING SUIT DYE

To the Editor:—I am reporting a case of pigmentation of the thigh following the running of a red dye from a bathing suit. The patient exposed herself to the sun, and some photosensitizing dye in the bathing suit produced this pigmentation. In reviewing the literature I have been unable to find a case of pigmentation from a photosensitizing dye. Would you please inform me whether such a case has been reported and also name the several red dyes which might have been used in dyeing this bathing suit? The pigmentation is similar to a "berloque" dermatitis.

I. LEWIS SANDLER, M.D., Washington, D. C.

ANSWER:—From the description, the case mentioned could well fit into the broad classification of "berloque" dermatitis. No report of such a case has been found, but the red dyes used in bathing suit manufacture fall within the eosin group, and it is conceivable that the eosins and erythrocin group have photosensitizing properties. For further technical information, consult *Occupational Affections of the Skin* by R. Prosser White (New York, Paul B. Hoeber, Inc.).

TRAUMATIC APPENDICITIS

To the Editor:—Further in regard to the report of Dr. Donald B. Rogers (*THE JOURNAL*, September 24, p. 1231) in reply to Dr. Royal H. Fowler (*THE JOURNAL*, July 30), I wish to mention the following case:

A WPA worker aged 37, giving no previous history of a disorder of the gastrointestinal tract, slipped and fell on a sewer main pipe with the weight and impact of the pipe he had been lifting coming down on his abdomen. He had been lifting this pipe, which weighs about 300 pounds, with four other men, and as he slipped their hold gave way and the patient's abdomen became wedged in between the rims of the heavy mains. This happened just before quitting time on a Saturday noon. He immediately felt a twinge in his side. He was able to reach home and vomited an hour after the injury. Pain became worse and for relief he took a little ginger and peppermint, thinking it was indigestion. That same night he vomited twice and on Sunday six times, with no relief of pain in the lower right quadrant of the abdomen. On this second day the patient seemed markedly ill; clinical and laboratory examinations pointed to a ruptured appendix. Operation confirmed this, showing a ruptured retrocecal appendix with spreading peritonitis. Recovery followed a stormy convalescence.

I ascribed this case to trauma, direct traumatic injury to the appendix with infection immediately superimposed at the site. I do not believe that a previous infection in the appendix is necessary to traumatic appendicitis but that the infection is carried on an injured area shortly after the injury. I do not believe that, as a requisite to diagnosis of traumatic appendicitis, the presence of previous disease, which would mean chronic appendicitis, is necessary, as upheld by the industrial commissions.

The WPA compensation commission in Washington holds that there is no such entity as traumatic appendicitis, giving this reason for ruling against this case. It sits in its cases, at least, as the final seat of judgment and establishes that there is no traumatic appendicitis.

EMIL S. GOODYEAR, M.D., Kingston, N. Y.

SPASMS OF LEGS AT NIGHT

To the Editor:—The reply given on page 2103 of the June 18 issue of *THE JOURNAL* to the physician who inquires about spasms of the legs at night seems somewhat incomplete. Nocturnal muscle cramps frequently occur in person beyond middle age and are not related to any form of peripheral vascular disease. Typical attacks occur in persons whose peripheral circulation is entirely normal. The cramps can be relieved in dramatic fashion by the administration of small doses of calcium lactate. In my experience with about thirty such cases 5 grains (0.3 Gm.) of calcium lactate an hour before meals has invariably relieved the symptoms. It is reported that from ten to fifteen drops of diluted hydrochloric acid in water with each meal will also act promptly in a similar manner. The following references will be of interest to the physician who inquired in regard to this condition:

Steven, R. A.: Muscle Cramps During Sleep, *THE JOURNAL*, Nov. 10, 1934, p. 1475.
Mills, C. A.: Muscle Cramps During Sleep, *THE JOURNAL*, Sept. 29, 1934, p. 1015.

SAMUEL SILBERT, M.D., New York.

Medical Examinations and Licensure

COMING EXAMINATIONS

STATE AND TERRITORIAL BOARDS

Examinations of state and territorial boards were published in THE JOURNAL, October 29, page 1685.

SPECIAL BOARDS

AMERICAN BOARD OF ANESTHESIOLOGY: An Affiliate of the American Board of Surgery. Written examination, Part I, will be held in various cities of the United States and Canada, April 8. Oral examinations for all candidates, St. Louis, May 13-14. Applications must be filed not later than sixty days prior to the date of the examinations. Sec., Dr. Paul M. Wood, 745 Fifth Ave., New York.

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY: Oral. St. Louis, Nov. 11-12. Sec., Dr. C. Guy Lane, 416 Marlboro St., Boston.

AMERICAN BOARD OF INTERNAL MEDICINE: Written examinations will be held in various parts of the United States, Feb. 20. Application must be received on or before Jan. 1. Sec., Dr. William S. Middleton, 1301 University Ave., Madison, Wis.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: Written examination and review of case histories of Group B applicants will be held in various cities of the United States and Canada, Feb. 4. General oral, clinical and pathological examinations for all candidates (Groups A and B) will be given in St. Louis, May 15-16. Applications must be filed not later than sixty days prior to date of examination. Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh (6).

AMERICAN BOARD OF OPHTHALMOLOGY: St. Louis, May 15. Applications must be filed before February 15. Sec., Dr. John Green, 3720 Washington Blvd., St. Louis.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: Memphis, Tenn., January. Sec., Dr. Fremont A. Chandler, 6 N. Michigan Ave., Chicago.

AMERICAN BOARD OF PEDIATRICS: Rochester, N. Y., November 13 and Oklahoma City, November 15. Sec., Dr. C. A. Aldrich, 723 Elm St., Winnetka, Ill.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: New York, Dec. 28-30. Sec., Dr. Walter Freeman, 1028 Connecticut Ave. N.W., Washington, D. C.

AMERICAN BOARD OF RADIOLOGY: St. Louis, May 11-14. Sec., Dr. Byrl R. Kirklin, 102-110 Second Ave. S.W., Rochester, Minn.

AMERICAN BOARD OF UROLOGY: New York, Jan. 13-15. Sec., Dr. Gilbert J. Thomas, 1009 Nicollet Ave., Minneapolis.

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: Parts I and II. Medical centers having five or more candidates desiring to take the examination, Feb. 13-15. Ex. Sec., Mr. Everett S. Elwood, 225 S. 15th St., Philadelphia.

Nebraska June Examination

Mrs. Clark Perkins, director, Bureau of Examining Boards, reports the written examination held at Omaha, June 8-9, 1938. An average of 75 per cent was required to pass. Eighty-one candidates were examined, all of whom passed. The following schools were represented:

School	PASSED	Year Grad.	Number Passed
Northwestern University Medical School.....	(1933), (1938)		2
University of Louisville School of Medicine.....	(1936)		1
Creighton University School of Medicine.....	(1938, 13)		13
University of Nebraska College of Medicine.....	(1936), (1937, 2), (1938, 62)		65

Four physicians were licensed by reciprocity from March 16 through July 26. The following schools were represented:

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
State University of Iowa College of Medicine.....	(1936), (1937)		Iowa
University of Michigan Medical School.....	(1928)		Michigan
New York Homeopathic Medical College and Flower Hospital.....	(1909)		New York

Ohio Reciprocity and Endorsement Report

Dr. H. M. Platter, secretary, Ohio State Medical Board, reports forty-two physicians licensed by reciprocity and five physicians licensed by endorsement July 19, 1938. The following schools were represented:

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
Loyola University School of Medicine.....	(1936)		California
Rush Medical College.....	(1919)		Michigan
(1936) West Virginia, (1936) Illinois	(1937)		
Indiana University School of Medicine.....	(1933)		Indiana
State University of Iowa College of Medicine.....	(1934), (1937)		Iowa
University of Kansas School of Medicine.....	(1937)		Kansas
University of Louisville School of Medicine.....	(1925), (1935), (1936), (1937)		
Johns Hopkins University School of Medicine.....	(1933), (1935)		Maryland
University of Michigan Medical School.....	(1931), (1936), (1937)		Michigan
Wayne University College of Medicine.....	(1938, 2)		Michigan
St. Louis University School of Medicine.....	(1937, 4)		Missouri
Washington University School of Medicine.....	(1934)		Missouri
University of Nebraska College of Medicine.....	(1935)		Nebraska
University of Buffalo School of Medicine.....	(1937)		New York
Temple University School of Medicine.....	(1936, 2)		Penna.
University of Pennsylvania School of Medicine.....	(1933)		Penna.
University of Pittsburgh School of Medicine.....	(1932), (1934), (1935)		Pennsylvania

Meharry Medical College.....	(1935)	Louisiana
(1931), (1934), (1936) Tennessee		
University of Tennessee College of Medicine.....	(1937)	Tennessee
Vanderbilt University School of Medicine.....	(1932), (1937)	Tennessee
University of Alberta Faculty of Medicine.....	(1929)	New York
Universität Bern Medizinische Fakultät.....	(1935)	Maryland

School	LICENSED BY ENDORSEMENT	Year Endorsement Grad.
Yale University School of Medicine.....	(1934), (1935)	N. B. M. Ex.
Harvard University Medical School.....	(1934)	N. B. M. Ex.
Tufts College Medical School.....	(1933)	N. B. M. Ex.
Duke University School of Medicine.....	(1935)	N. B. M. Ex.

Book Notices

A Manual on Pharmaceutical Law Together with Appendices Containing Important Laws of Congress, the Uniform Narcotic Drug Law, and Other Laws Relating to Pharmacy. By C. Leonard O'Connell, Dean of the Pittsburgh College of Pharmacy, University of Pittsburgh, Pittsburgh, and William Pettit, Member of the Pittsburgh Bar. Cloth. Price, \$2.50. Pp. 196. Philadelphia: Lea & Febiger, 1938.

Few fields, the authors say, have as frequent and daily contact with rules and regulations as the profession of pharmacy; and he certainly proves his case, as may be seen from the chapter headings, which cover government and the regulation of pharmacy, state regulation, federal regulation, the pharmacist's liability for negligent acts, the pharmacist's liability for negligence of the employee, other rights and liabilities, contracts relating to the sale of drugs, bankruptcy, insurance and trade restraints. There is an appendix dealing with the Harrison Narcotic Law, the federal Food and Drugs Act, the federal criminal law relating to nonmailable matter, and other important laws. In chapter I the author explains that the federal government, in respect to delegated powers, is supreme but that it is restricted to a far greater extent than the state governments, which in the exercise of their "police power" may variously regulate the practice of pharmacy and the sale of drugs and poisons. To the physician the question of the ownership of prescriptions is of special interest: a question not definitely decided by the courts. Reading between the lines, it is obvious that the customer owns the prescription until it is filled, then the pharmacist shall keep the prescription on file for a period of years, usually five. For such a period, at least, the customer cannot demand return of his prescription. No decision is available as to whom the prescription belongs after the lapse of the five years, but common sense should dictate that at the end of this time the pharmacist may destroy the prescription if it is not called for at that time. Pharmacists are prohibited from practicing medicine, but that means they are really merely prohibited from making diagnoses and from an actual application of remedies. The pharmacist in instructing as to the use of a medicine after he has sold it would not be diagnosing or treating disease.

Nouvelle pratique dermatologique. Publiée par MM. Darier, Sabouraud, Gougerot, Millan, Pautrier, Ravaut, Sézary, Clément Simon. Secrétaire général, Clément Simon. Tome VII: Maladies des annexes de la peau. Dermatoses non classées. Dermatologie comparée. Par MM. Ch. Audry et al. Boards. Price, 300 francs. Pp. 896, with 407 illustrations. Paris: Masson & Co, 1936.

The first 240 pages of volume VII are the contributions of Sabouraud alone and in collaboration with Pignot on the hair and sebaceous glands. There is so much disagreement among dermatologists as to what constitutes pityriasis simplex, pityriasis steatoides and the seborrheic states that every one should take advantage of the opportunity of reading this clear and logical presentation of the subject. According to Sabouraud, pityriasis of the scalp is an exfoliation of the corneous layer of the skin due to the Pityrosporon of Malassez. The two photographs on pages 28 and 29 showing the similarity between sections of pityriasis simplex and pityriasis versicolor are convincing. Most of the textbooks describe seborrheic dermatitis as beginning in the scalp and spreading down over the face. Sabouraud reverses the sequence of events and insists that the seborrhea begins on the face and spreads to the scalp. The apparently oily masses formed in pityriasis steatoides are not only not greasy but contain less oil than is found in normal exfoliation of the corneous layer. "The patient is aware that his scalp quickly becomes dirty and that when he scratches it with his nails he removes dirt which has a greasy appearance and

which most dermatologists consider to be glandular secretion, in other words seborrhea, but which as a matter of fact is a surface exfoliation infiltrated by serum exuded from the surface of the epidermis. Such a state is accompanied by a loss of a few hairs but in slight proportion. There is very little alopecia even with pityriasis steatoides. The alopecia is really seborrheic, that is to say in connection with the infection by the microbacillus" (p. 35).

Sabouraud discusses at length seborrheic eczema of Unna. He gives Unna credit for having observed the sequelae of the two forms of pityriasis in the scalp but says that he was at fault in ascribing these changes to his morococcus. "The synthesis which he made was in every way remarkable, and the only reproach which one can make is the insufficient description of his microbe and the insufficient differentiation with the other cocci of the skin. It is by reason of the paucity of his bacteriologic methods that so many errors survived" (p. 38). The morococcus, according to Sabouraud, was nothing more than various kinds of staphylococci. "From then on all pustules were declared by him morococci and little by little the field of seborrheic eczema extended indefinitely." Unna also failed to realize that in pityriasis simplex or steatoides a secondary infection might occur to account for this weeping and crusting. "This superinfection Unna still insisted was seborrheic eczema and he failed to recognize the fact that it was a transitory secondary streptococcal infection" (p. 44). "About the seventeenth year one may see the seborrheic infection of the temples invade the scalp about the borders, beneath the scales of the pityriasis, and one is confronted by a complexus of three infections: the spore of Malassez, the polymorphous coccus and the microbacillus. In this way seborrhea of the scalp begins."

In the discussion of the treatment of hypertrichosis it is interesting to note what is said concerning the use of thallium acetate. "The local use of thallium acetate has been much criticized in recent years. It was one of us (Sabouraud, *Entretiens dermatologiques à l'Ecole Lailler, 1^{re} série*) who suggested it twenty years ago and we have never seen its use followed by accidents. But we must know how and when to use it and also the results one may expect. Never can one expect to obtain more than one-half diminution of the existing hypertrichosis. The disgrace thereby becomes only half as visible, but when it is slight the result is sufficient. A pomade of acetate of thallium should never exceed 2 per cent and never should the patient use more than the size of a small pea in all. It is applied by massage over the region. After the massage the hands are washed with soap. . . . This treatment should be repeated each evening. For three months the results may seem negligible but each month thereafter there is improvement."

In some ninety-two pages the entire subject of alopecia, including pelada and pseudopelada, is discussed. Much of this material is to be found in Sabouraud's book on the alopecias (*Pelades et alopecies en aires, Paris, Masson & Cie*). As he is the recognized authority on alopecia areata, it is refreshing to read the closing sentence: "All of which proves that there remains much to learn on the subject."

Audry, who has since passed away, discusses the disorders of the sweat glands. Following this is a dissertation by Chatellier on hydrosadenitis, granulosis rubra nasi and anidrose avec hypotrichose et anodontie.

The diseases of the nails are treated at length by Milian. The subject is so well covered and the illustrations are so admirable that no comment is necessary. The chapter should serve for years to come as an authoritative reference on onychia.

Gastinel and Solente give a highly satisfactory presentation of erythema multiforme with magnificent illustrations in color as well as in monochrome. Following this Solente describes érythèmes figurés chroniques. This most difficult group of dermatoses is handled in a masterly way and is accompanied by excellent illustrations and five pages of bibliography.

Dermatitis herpetiformis is well set forth by Tzanck and Cord and is followed by an article on hydroa vacciniforme by Tzanck and Pautrat. This group is ended by Lévy-Solal and Pautrat on herpes gestationis.

A feature of this volume is the work of Pautrier on lichen planus and abnormal lichenification. Those who are familiar

with the voluminous contributions made by this author to the subject need not be told that he has completely covered these dermatoses in the 130 pages. There are sixteen plates in color illustrating his original investigations made on lichen planus. Any further comment on the work of this author would be superfluous.

To Margat falls the responsibility of covering the subject of psoriasis. In the 112 pages allotted to him he gives an excellent account of his ability. The illustrations and the bibliography added to a particularly clear style of exposition make this part of the volume most admirable. The description of psoriasis arthropathique is the most satisfactory that comes to mind. There are three roentgenograms which contribute greatly to the clear understanding of this complicated feature of psoriasis.

Cohen writes an excellent exposition on pityriasis rubra pilaris in a few pages. The two illustrations, one in monochrome and one in color, are strikingly accurate.

Another feature of this volume is the contribution of Civatte on parapsoriasis. The bibliography is scanty but the photographs both clinical and micrographic are numerous and of the highest quality. The exposition, as is to be expected of Civatte, is perfect.

The exfoliating erythrodermas by Nanta and urticaria pigmentation by Gastou are complete in every way.

The most arresting feature in this volume is the closing 141 pages by Henry, professor of parasitology and dermatology of the veterinary school of Alport and Bory of Saint-Louis on comparative dermatology. Their opening statement is as follows: "We define comparative dermatology as the study of animal dermatoses which may have something in common or comparable with human dermatoses, taken as a point of departure or of return." The authors discuss successively the parasitic dermatoses due to insects, Acarus, Demodex, scabies, cutaneous worms, protozoans, Epidermophyton, Trichophyton and all the other diseases common to man and animal. The illustrations and the bibliography are of the highest order. No one should neglect an opportunity to read intensively this section of volume VII.

Clinics on Secondary Gastro-Intestinal Disorders; Reciprocal Relationships. By Julius Friedenwald, M.D., Theodore H. Morrison, M.D., Clinical Professor of Gastro-Enterology, University of Maryland School of Medicine, Baltimore, and Samuel Morrison, M.D., Assistant Professor of Gastro-Enterology, University of Maryland School of Medicine, Baltimore. Cloth. Price, \$3. Pp. 251. Baltimore: William Wood & Company, 1938.

Any book that bears the name of Julius Friedenwald will be read with interest and respect by his colleagues, who know that he has had an enormous experience and that in spite of his years he remains young in outlook on science and life. This book was written primarily for the medical student and general practitioner, the idea being to put together a few essays on some of the conditions outside the stomach and intestine which commonly produce indigestion. Among these are heart disease, pulmonary tuberculosis, liver and gallbladder disease, focal infection, genito-urinary disease, disease of the female pelvic organs, endocrine dysfunctions, menopausal upsets, syphilis, hematopoietic and dietary deficiency disturbances, nervous disturbances, skin diseases, eye diseases and food allergy.

On looking through the book one finds much that is interesting and much that is sane and helpful. There are good bibliographies at the end of the chapters. Obviously in a short book like this the expert will always see gaps and places in which he thinks he could have written more, chosen the subject matter more wisely or quoted better authorities. The principal criticism that might be made is that in a number of places the information given is not sufficient so that the physician seeking information can gain clearcut impressions of the essential points which will help him in diagnosis or guide him in treatment. For instance, in the section on heart disease there is a good deal about the easily recognized disturbances of digestion which go with decompensated valvular heart disease. Actually, where a physician needs help most is in attempting to recognize the digestive disturbances produced by a narrowing coronary artery some time before the patient drops dead. What is needed is help in differentiating gas in the splenic flexure that is pressing up on the heart from the sensation of gas that is being produced by a failing heart.

On the whole, however, the book is interestingly and well written and contains much information. It should be on the shelf of every man who is trying to fit himself to be a better gastro-enterologist. One of the surest signs of a poor specialist is a tendency to accept everything as grist to his mill and to assume that the symptoms complained of by all patients who come to him are due to disease in his pet organ. Conversely, the surest sign of a good specialist and one who has attained unto wisdom is a readiness to say to many patients "Your symptoms may be in my field, but their source is not. Go you out unto another specialist to whom I shall direct you." This little book is designed to help in the development of wise gastro-enterologists.

Úlcera gástrica y duodenal: Estudio clínico y radiológico. Especialmente de las alteraciones patológicas de la mucosa gastroduodenal. Terapéutica. Por Jose M^a. Orledo Bustos, adscrito a la Cátedra de clínica médica. Prólogo del Dr. Marilino R. Castex, miembro de la Academia nacional de medicina. Cloth. Pp. 674, with 510 illustrations. Buenos Aires: Librería y editorial "El Ateneo," 1938.

This large volume is another one of the valuable contributions to modern medicine which emanate periodically from the Medical Clinic of the National University at Buenos Aires under the leadership of Professor Castex. After certain general considerations, the author discusses the various theories of the cause of duodenal ulcer and its frequency and predisposition, anatomy, physiology and symptomatology. Some 240 pages are devoted to the radiologic study of gastric and duodenal ulcer. The remainder of the book deals briefly with gastroscopy and at some length with complications of gastroduodenal ulcer, its diagnosis, prognosis and treatment, nonsurgical and surgical. Finally consideration is given to the hygiene of the gastrectomized patient and the diagnosis and management of some of the complications. Perusal of the text does not reveal any innovations; there is a complete and satisfactory discussion of standard medical conceptions and practice in the management. Many of the radiologic illustrations are amplified by drawings. All the illustrations are clear. One finds the text ample and reliable. The radiologic symptoms are everywhere correlated with the other symptoms and signs. The work constitutes a real clinical contribution which should redound greatly to the credit of the author and to the eminent Argentine clinic which made this extensive work possible.

A Text-Book of Pathology. Edited by E. T. Bell, M.D., Professor of Pathology in the University of Minnesota, Minneapolis. Third edition. Cloth. Price, \$9.50. Pp. 894, with 414 illustrations. Philadelphia: Lea & Febiger, 1938.

The new edition of Bell's textbook has been thoroughly revised and 123 pages of new or corrected material, forty-eight illustrations—mostly excellent photomicrographs—and more bibliographic references have been added. As in the 1934 edition, the first part of the text is concerned with general pathology, the rest with the pathology of special organs. The same four collaborators have contributed chapters on special subjects. The Mycoses by J. S. McCartney, M.D., is a good brief discussion of the common fungous diseases, and material on moniliasis has been added. McCartney also contributed the chapter on diseases of the liver and gallbladder, which includes new material on infectious jaundice and von Gierke's disease. The chapter on diseases of the spleen, by C. J. Watson, revised by Bell, gives a useful classification of splenic disorders, prefaced by a discussion of splenic functions and anatomy. The discussion of diseases of the heart by B. J. Clawson has a good summary of our present knowledge of rheumatic heart disease, a subject to which its author has devoted special study. Some readers might object to the grouping of malignant and ulcerative endocarditis with endocarditis lenta in the discussion of subacute bacterial endocarditis. The statement is made that death often occurs in coronary sclerosis without thrombosis, but there is no mention of the mechanism stressed by Leary, rupture of an atheromatous plaque with embolization of multiple branches, which may account for some of these fatalities. Diseases of the Blood is an excellent chapter by an expert hematologist, Hal Downey. The material on the erythrocytes and the anemias has been brought in line with recent work. Nonleukemic disorders with quantitative and qualitative changes in the blood cells are well discussed. The section on the leukemias is

simple, brief and helpful. Perhaps the lack of confusing detail is explained by the final section on the origin and relations of the blood cells, with its lucid criticism of rigid hematologic classifications. Bell's own contribution—and the major part of the book—has been carefully revised. Among the many subjects treated with greater detail are constitutional and hereditary factors in disease, calcium and chloride metabolism, the pathology of vascular diseases, endocrine disorders and virus diseases. The general discussion of tumors is good. Much new material has been interpolated in the various chapters and there are at least brief accounts of many of the rarer or recently identified conditions, such as nontropical sprue, regional ileitis, lipid pneumonia and glomus tumors. Especially valuable, coming from a man who has studied renal pathology so thoroughly, is the chapter on diseases of the urinary system. This is prefaced by an excellent discussion of pathologic physiology. The revised classification and discussion of renal diseases is good from both the morphologic and clinical-pathologic points of view. Probably it will not meet universal approval, and Bell himself may wish to make further revision in the next edition. However, this is a real contribution toward clarifying a very confused subject. Considered as a whole, this improved textbook with its expanded bibliographic material should prove a convenient and remarkably complete brief reference work and will probably find considerable use as a textbook for students. The relatively greater emphasis on systemic pathology and the briefer discussion of general pathology and pathologic principles perhaps will bar widespread employment as a beginner's textbook. This balance however makes it a more useful textbook for the advanced student and the practitioner.

Action hypoglycémiant de l'insuline chez le chien sous l'influence de la pancréatectomie, de la dégénérescence exocrine du pancréas après ligature des canaux et du jeûne prolongé. Par Raymond Castagnou, docteur en pharmacie. Paper. Pp. 156, with 26 illustrations. Bordeaux: Imprimerie E. Drouillard, 1936.

Dr. Castagnou's monograph describes a number of excellently planned and executed experiments on the hypoglycemic action of insulin on dogs. The study is in several parts. The first is devoted to the investigation of the characteristics of hypoglycemic curves in the normal dog after intravenous and subcutaneous injection of insulin. In executing these, as well as in the subsequent experiments, the author made use of the method devised by Trinquier and modified by Aubertin. He also describes a new measure for the intensity of the hypoglycemic reaction to injected insulin, which is intended to supplement the index of assimilation of Norgaard and Thyssen. This is the angle formed by lines drawn tangent to the assimilation and restoration curves.

A second series of experiments concern themselves with the variations in the hypoglycemic action of insulin, after partial or total pancreatectomy. The principal result here is the observed regularity of the assimilation curves which follow the operation, in contrast to the frequent oscillation observed in similar curves for the normal dog. The pancreatectomy influences all the measures of the hypoglycemic reaction except the relative percentage of fall from the initial blood sugar content to that of the maximal drop after insulin injection. This percentage of drop in the assimilation curve seems to be constant whatever the initial values, and the author's inference from this is that the hypoglycemic action of insulin is related principally to the time during which the insulin continues to act.

In order to determine whether hypoglycemic reaction of insulin might not be linked with the external pancreatic secretions, several experiments involving ligation and section of the pancreatic ducts were made. Results showed that retention of the external secretions in no way influenced the exogenous action of insulin. The author concludes from this that the increased hypoglycemic action of insulin after removal of the pancreas cannot be ascribed, as others have held, to the suppression of the external secretions of the pancreas. The author is likewise of the opinion that in normal conditions also the external pancreatic secretions do not exercise any considerable influence as a regulatory mechanism of the secretions of the organ.

Animals deprived of their glycogen reserve, as a result of fatty degeneration of the liver or of prolonged inanition, fail to show normal hypoglycemic curves. There is an entire lack

of demarcation between the primary and secondary restoration curves. This is explained as due to the impairment of the mechanism which normally excites islet secretion.

The author offers a number of explanations with regard to the causes of various hypoglycemic reactions following injection of insulin, and a new hypothesis as regards their possible bearing on the diabetic mechanism. As regards the latter, Dr. Castagnou suggests that diabetes does not impair the processes, per se, which mediate hypoglycemia but merely retards, for a considerable time, the rate at which these take place. It is the latter secondary fact which accounts for the prolonged action of insulin in diabetes.

The monograph is documented with 108 references to current literature.

Glaister's Medical Jurisprudence and Toxicology. Edited by John Glaister, M.D., D.Sc., Barrister-at-Law, Regius Professor of Forensic Medicine, University of Glasgow. Sixth edition. Cloth. Price, \$8. Pp. 747, with 115 illustrations. Baltimore: William Wood & Company, 1938.

Sooner or later every active medical practitioner may be called as a witness to render such service as the law may demand from him. Every medical man, therefore, should know what legal demands may be made on him and the more relevant facts on which he may be called to express opinions. This volume provides a dependable guide. The more noteworthy chapters are those devoted to cases of homicide, causes of insensibility, lunacy, insanity, monoxide poisoning and incest. The section on toxicology is complete. Fundamentally and in principles the entire book is sound in all its comment and instruction. Written by an English author experienced in British procedures and courts, he has devoted much space to the quotation of English laws and procedures. These are of course not applicable in this country. The American physician must therefore go further and supplant American laws for the quoted laws. However, there is so much of value presented clearly and correctly that the book is valuable for physicians in this country. It will also reveal the lag in forensic medicine and the need for prompt reforms in our country.

Le traitement radiologique de l'actinomyose. Par Axel Renander. Communication de Radiumhemmet et de l'Institut roentgen de l'Hôpital Serafimer, Stockholm. Chefs: M.M. G. Forssell et E. Berren. Acta radiologica, Supplementum XXXV. Paper. Price, 8 Swedish crowns. Pp. 75. Stockholm: P. A. Norstedt & Söner, 1937.

An excellent historical account of our knowledge of actinomycosis is afforded in this monograph, which deals with the localization of the disease and the various methods of treatment, especially with potassium iodide. Credit is given to Bevan for the first case in which treatment was given with the x-rays. In 1905 Bevan described six cases of actinomycosis treated successfully with the roentgen ray. Since then numerous authors have reported favorably. Fifty-two verified cases of actinomycosis treated by Forssell and his colleagues in Stockholm between 1915 and 1932 form the basis of this work. Forssell's technic is given in detail, both for x-rays and for radium. Radium was never used alone but as an adjunct to roentgen treatment. Cure was obtained in 83 per cent of the cervicofacial lesions and in 38.3 per cent of the abdominal cases. There were no survivals among the genital or thoracic cases. Potassium iodide did not seem important as an additional method of treatment; there was no difference in the rapidity of cure in cases in which potassium iodide was not prescribed.

Kurs meditsinskoy rentgenologii dlya vrachey i studentoy. Pod redaktsiyey Prof. S. A. Reynberga. [Text Book on Medical Roentgenology for Physicians and Students.] Cloth. Price, 14 rubles. Pp. 784, with 503 illustrations. Moscow & Leningrad: Gosudarstvennoe Izdatel'stvo Biologicheskoy i meditsinskoy literatury, 1938.

This is a textbook on medical roentgenology written for the general practitioner and the medical student. It contains a discussion of the physics of the roentgen rays, the principles underlying the roentgen technic and roentgenologic investigations. There are chapters on the general and the local roentgenologic diagnosis as related to pathologic anatomy, physiology and clinical knowledge. The text further contains a discussion of the biologic properties of roentgen rays and of the principles of general and local roentgenotherapy. The text does not attempt to be anything more than a guide for the medical student and

for the general practitioner and, at best, an introduction to the study of roentgenology for the future specialist in this field. As such it is quite satisfactory and fills a gap in the armamentarium of the Russian physician.

Die tuberkulöse Lungenblutung: Entstehung, Klinik und Behandlung. Von Dr. med. Friedrich Hasselbach, Oberarzt. Nr. 67, Tuberkulose-Bibliothek, Beihette zur Zeitschrift für Tuberkulose. Herausgegeben von Dr. Franz Redeker, Oberregierungs- und Obermedizinalrat, Berlin, und Dr. Karl Diehl, dirigierender Arzt, Sommerfeld. Paper. Price, 6.60 marks. Pp. 45, with 31 illustrations. Leipzig: Johann Ambrosius Barth, 1938.

Most of the illustrations are made from roentgenograms of chests. The author discusses the types of hemorrhage of pulmonary tuberculosis with reference to the source of blood and also presents the pathologic changes and theories concerning hemoptysis. With reference to the time of year, he finds that most hemorrhages occur in December. They are also frequent in April and July. The effects of various substances, such as tuberculin, insulin and vitamin C, are discussed, as well as treatment by artificial pneumothorax, rest, sedatives and other usual methods. He calls attention to the fact that pulmonary hemorrhage may be the first external evidence of tuberculosis in the group he classifies as inflammatory or allergic lesions. This work contains a good bibliography, and all the material is well presented.

Hernia: Anatomy, Etiology, Symptoms, Diagnosis, Differential Diagnosis, Prognosis, and the Operative and Injection Treatment. By Leigh F. Watson, M.D., Member of Attending Staff of California Lutheran Hospital and Methodist Hospital of Southern California, Los Angeles. Second edition. Cloth. Price, \$7.50. Pp. 591, with 281 illustrations. St. Louis: C. V. Mosby Company, 1938.

This edition fulfils the need for an authoritative work on the new developments in the treatment of hernia. The treatment by injection is covered in detail. No extravagant claims are made for the injection method. The indications outlined as to the applicability of the injection method are conservative and conform with the best opinions on this subject. The technical steps are clearly outlined, particularly in the use of the injection method in inguinal and umbilical hernias. For completeness the author has described the technic of the treatment of femoral and incisional hernias by injection but properly does not encourage its use in these types of hernia. A chapter on trusses, while not as complete as might be expected, covers the essential points of good truss fitting. The description of operative technics is excellent. The more popular procedures in the operative treatment of every type of hernia are carefully and accurately described and illustrated by many fine drawings. The use of local anesthesia is advocated and the steps in the induction of such anesthesia are well outlined. There is an excellent chapter on the medicolegal and industrial aspects of hernia. A complete bibliography at the end of each chapter makes this book particularly attractive for the medical student. Throughout the entire book it is evident that the writer has the point of view of the general practitioner, doing limited surgery on hernia, as well as that of the surgical specialist who desires a complete reference work. This book should be a valuable addition to the library of the medical student, the general practitioner and the surgical specialist.

Handbook of Practical Bacteriology: A Guide to Bacteriological Laboratory Work. By T. J. Mackie, M.D., D.P.H., Professor of Bacteriology, University of Edinburgh, Edinburgh, and J. E. McCartney, M.D., D.Sc., Director of Research and Pathological Services, London County Council. Fifth edition. Cloth. Price, \$4. Pp. 586, with illustrations. Baltimore: William Wood & Company, 1938.

This little guidebook to bacteriologic laboratory work is now in the fifth edition since 1925. Many useful technics are described, including the care of animals and the methods of animal inoculation and necropsy. One appendix describes methods of filtration and the other the scheme of colors for identifying sugar mediums.

Epilepsiya. Pod redaktsiyey Kh. G. Khodosa. [Epilepsy.] Paper. Price, 5 rubles. Pp. 239. Irkutsk: Irkutskoe Oblastnoe Izdatel'stvo, 1938.

The material embraces cases of epilepsy treated between 1921 and 1933. The monograph deals with clinical aspects of the disease and offers neither new observations nor new theories.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Liability of Hospital for Improper Treatment by Layman.—Hendrickson had a sore on his lower lip, which, according to the reported decision, had been a small superficial cancer that had been cured by treatment at several hospitals. He continued to suffer, however, from the after effect of the radium treatment which he had received. Rigley, a layman, arranged a meeting with Hendrickson and told him he could cure the "crab" on his lip in thirty-one days. He claimed he had brought over from Ireland an old family remedy for the cure of cancer, a salve, and displayed Irish newspaper accounts of cures allegedly accomplished by its use. He displayed also a bottle which he said contained a cancer that had been removed from the face of one Smith, at whose home the meeting was held by Rigley's contrivance, although later the court said that there was no evidence that Smith ever had a cancer.

Hendrickson then consulted a physician, a relative, who advised against any treatment except treatment at a hospital and under a physician's supervision. Rigley, however, caused Hendrickson to be examined by a Dr. Hodkin, who later became one of the defendants. He, according to the published decision of the court, after a superficial examination informed Hendrickson that his case was a serious one and that a cure would cost \$10,000, which amount he later reduced to \$3,000. Hendrickson was subsequently admitted to the defendant hospital, operated by the Park East Operating Corporation, and there Dr. Hodkin introduced Rigley to the superintendent as "the man who has the cure."

There, in the presence of Dr. Hodkin, Rigley ground up a substance, later shown to be an arsenic compound, and made a paste. Because Dr. Hodkin disagreed with Rigley as to the exact area to which the paste should be applied, he left the room and did not return for two weeks. After Dr. Hodkin's departure, Rigley scratched Hendrickson's chin until blood appeared and then applied the paste and covered it with a bandage. He told a nurse employed by the hospital, to whom he admitted he was not a doctor, that the paste "contained white arsenic and herbs; that it was the most powerful poison in the world, but that his herbs controlled it." Two or three days later Hendrickson's face became swollen and painful. Rigley then "put new skin on the lip where the abrasion was in an effort to stop the flow of saliva." On Rigley's instructions, the nurse administered aspirin and whisky to relieve the pain. On one occasion a hemorrhage had to be stopped by a house physician. The paste, which medical witnesses believed should not have been allowed to remain on longer than eighteen hours, was kept on for twenty-one days. When Hendrickson left the defendant hospital, at the superintendent's request, because his hospital bill was not paid up to date, "the flesh had been eaten away from the lip and chin," "there was no lip or chin left, and his teeth fell out."

Hendrickson brought suit and obtained a judgment for \$40,000 against the defendants, Rigley, Dr. Hodkin and the hospital. On appeal by the defendant hospital, the supreme court of New York, appellate division, second department (250 App. Div. 619, 294 N. Y. S. 982, abstracted, *THE JOURNAL*, Jan. 1, 1938, p. 74), reversed the judgment against the hospital. Hendrickson thereupon appealed to the Court of Appeals of New York.

The medical testimony, said the Court of Appeals, showed that the treatment administered by Rigley was a competent producing cause of the appellant's condition. Furthermore, the evidence presented by Hendrickson, the appellant, justified the jury in finding that the hospital admitted the appellant "knowing that the purpose of his being there was for an improper treatment by a layman, 'the man who has the cure';" that the hospital records showed that Rigley personally treated the appellant; that nurses, hospital physicians and the superintendent of the hospital knew that the appellant was being treated by Rigley without the supervision of a physician; that the superintendent knew that the paste used in the treatment was a

preparation whose composition was known only to Rigley; and that the superintendent, knowing what was going on, stated: "We will have to play along with him [Rigley]. If everything comes out all right, we will be all taken care of." The superintendent knew or should have known that Rigley was engaged in the commission of a crime by unlawfully practicing medicine, a crime of which he was later convicted, and that the hospital, in affording its facilities for pay, was aiding and abetting him in the performance of a criminal act. The basis of the liability was not the negligence of the doctor or nurse in charge but the wrongful conduct of its superintendent, acting within the scope of his authority, in permitting the facilities of the hospital to be used for the commission of criminal acts in violation of a duty owed to the patient.

In the judgment of the Court of Appeals, the supreme court, appellate division, erred when it held the hospital not liable on the theory that the only fault was that of the doctor and nurse. Accordingly, the Court of Appeals reversed the judgment of both lower courts and granted a new trial.—*Hendrickson v. Hodkin et al.* (N. Y.), 11 N. E. (2d) 899.

Workmen's Compensation Acts: Compensability of Cerebral Hemorrhage Following Exertion.—Neas, suffering from high blood pressure, in the course of his employment as a lineman for a power company climbed and descended two poles in rapid succession. After descending the second pole he staggered toward his truck and slumped down in the seat. He was immediately taken to a hospital, where he died within a few hours of a cerebral hemorrhage. The claimants, his wife and children, denied compensation under the workmen's compensation act by the industrial accident board of Texas, filed suit in a state court to set aside the board's award and to recover compensation, but the suit was removed to the federal district court. All the medical witnesses agreed that the cause of death was a hemorrhage due to a rupture of weakened arterial walls in the brain. They agreed that physical exertion would cause an increase of blood pressure and could precipitate such a hemorrhage but that such a hemorrhage could occur without previous violent exertion. In answer to hypothetical questions some physicians expressed the opinion that the climbing and descending of two poles in succession could and did cause the hemorrhage to begin immediately, while others thought that because such exertion was habitual to the workman in this case it did not cause the hemorrhage. From a verdict by the jury in favor of the claimants and from the resulting judgment, the insurer appealed to the circuit court of appeals, fifth district.

The main question was whether the evidence authorized submission of the claim to the jury. The jury, said the circuit court of appeals, could find from the evidence that the workman climbed the two poles in immediate succession and that his hemorrhage was precipitated by that exertion. The hemorrhage, though not outwardly visible, was a "damage or harm to the physical structure of the body" within the meaning of the term "injury" as defined in the Texas workmen's compensation act. The act requires that the injury shall have originated in the work of the employer while the employee was engaged in it, but the jury could reasonably find that the climbing of the two poles was the direct and immediate cause of the arterial rupture and that that rupture would not have occurred but for such exertion.

The insurer argued, however, that in order to recover under the Texas workmen's compensation act there must be an accident in the course of work, something that unexpectedly causes unusual exertion and overstrain, and that there was nothing to show that anything of the sort occurred. But, said the circuit court of appeals, the Texas workmen's compensation act does not expressly require that an accident shall have happened. This very court, in *Salinas v. New Amsterdam Casualty Co.*, 67 F. (2d) 829, used the expression "accidental injury," describing such an injury as one occurring unexpectedly and not in the natural course of events and susceptible of being traced to a definite time, place and cause. The arterial injury which happened to Neas was not a wilful injury, was unexpected and not in the usual course of events and was traced to a definite time, place and cause. The test is not whether the exertion or strain which immediately caused the injury was unusual in the course of the work in which the injured employee was engaged

but whether such exertion was beyond that which members of the public not so employed ordinarily would incur. If exertion was not unusual in the latter sense, the employer is not to be charged with the injury even though it happened while the employee was at work. If, however, the employee as a member of the public would ordinarily not incur such a strain as that which injured him, the injury is to be attributed to his employment even though a disease condition may have made him more vulnerable. In this case Neas was required by his employment to climb poles, involving an exertion far greater than members of the public would ordinarily undergo. If that exertion then and there caused a brain hemorrhage which would not have otherwise happened, there was an injury originating in the work for which the statute requires industry to make compensation.

The judgment in favor of the claimants was accordingly affirmed.—*Fidelity & Casualty Co. of New York v. Neas*, 93 F. (2d) 137.

Adjudication of Insanity: Right to Trial by Jury.—The appellant was adjudged insane by the commissioners of insanity of Monroe County, Iowa, and ordered committed to a state hospital. She appealed to the district court of that county and from an order of the district court denying her a trial by jury she appealed to the Supreme Court of Iowa, contending that that denial invaded her right of trial by jury guaranteed by the constitution of Iowa.

The purpose of an inquisition of insanity, said the Supreme Court, is to aid and assist the individual, to provide means whereby the state may protect its unfortunate citizens and to furnish hospitalization and treatment in order that the insane may have an opportunity to rehabilitate and readjust themselves as useful and happy citizens. Such an inquisition is not a criminal proceeding in any way. Confinement of persons who are mentally sick is not intended as punishment but only to provide them with an environment that may possibly cure their disease and return them to society. Accordingly, the Supreme Court, two justices dissenting, affirmed the judgment of the lower court, denying the appellant the right to a trial by jury.—*In re Brewer (Iowa)*, 276 N. W. 766.

Workmen's Compensation Acts: Liability for Expense of Exploratory Operation.—On January 7 Bochot, while shoveling snow from the roof of a shed in the course of his employment by the defendant, slipped and fell. He sustained "a back sprain," which healed by February 20. From ten to thirty days after his fall he noticed pain and swelling on the right side of his abdomen. His condition became progressively worse and an immediate operation was recommended. His attending physicians were of the opinion that the operation would prove or disprove their belief that his condition was not due to the accident. Bochot was informed that the industrial commission would assume all costs "if it appeared, after the operation, that his condition was caused, or aggravated, by the accident," but that if it appeared that his condition was not attributable to the accident he would have to bear the costs. The operation was performed and a hydronephrosis of one kidney was found. This, the operating physicians concluded, had been present long before the accident and had not been aggravated by it. The claimant brought proceedings before the industrial commission under the workmen's compensation act of Arizona. From an award of the commission granting compensation for temporary disability from January 9 to February 20, the period during which he suffered from a strain of his back, but denying compensation for any time thereafter, he appealed to the Supreme Court of Arizona.

If it appeared from the record, said the Supreme Court, that the operation had been performed at the request of the commission to satisfy it as to the cause of the claimant's condition, the court would be inclined to hold that the commission was liable for the expenses caused by its request. The evidence did not show, however, that the operation had been performed at the commission's request. The situation prior to the operation was that on the information then available to it the commission would have had to deny any request for compensation further than that which it had awarded. An operation was necessary to save the claimant's life regardless of the cause of his condition. On this state of the affairs the commission went as

far as it had any right to go when it informed the claimant that it would pay the expenses of the operation if it revealed that the accident had caused or aggravated his condition. Since the testimony of the operating physicians showed that the accident had not caused or aggravated the claimant's condition, the court concluded that the commission had properly refused to award additional compensation. Accordingly, the award of the industrial commission was affirmed.—*Bochat v. Prescott Lumber Co. (Ariz.)*, 74 P. (2d) 575.

Workmen's Compensation Acts: Death Caused by Exertion and Myocardial Disease Compensable.—The deceased, a carpenter, in the course of his employment assisted his fellow workmen in lifting and carrying window sashes and lumber, the individual pieces ranging in weight from 75 to 100 pounds. The thermometer stood at 90 F. in the shade, and the men worked in the sun's rays and under pressure. The deceased seemed to be exhausted. He perspired very freely and a fellow workman had "to keep pushing him along." He went into the cellar to get a drink of water. Five minutes later he was found unconscious and shortly thereafter he died. His widow sought compensation under the workmen's compensation act of New Jersey.

A physician testifying on behalf of the widow said that the death, caused by "syncope due to myocardial heart disease," was the result of the exertion incident to employment. A physician testifying on behalf of the employer stated, however, that while he believed that death was due to heart disease he could find no evidence of any accident and that the exertion of employment had no relation to the death. On cross examination he admitted that the exertion "may have been more liable to have something to do with it" and that exertion will aggravate a myocardial condition. Another physician called by the employer admitted that, when heart disease exists, such exertion as that of the deceased, coupled with the extreme heat of the day, could cause death. The workmen's compensation bureau nevertheless denied compensation, holding that the claimant had failed to prove that her husband died as the result of an accident arising out of and in the course of his employment. She appealed to the court of common pleas, which reversed the decision of the workmen's compensation bureau and awarded her compensation. The employer thereupon brought certiorari to the supreme court of New Jersey.

Unquestionably, said the supreme court, the deceased workman had a preexisting heart disease. While the testimony indicated that he might have died at any time, there was also testimony supporting the conclusion that there was a causal relation between the death and the heavy work in which the deceased was engaged, the extreme heat of the day and more or less continuous exertion. The employer stressed the fact that the work done by the workman was the same work as was done by others and therefore was not unusual. This argument, said the court, is without merit, since the proofs support the conclusion that the workman showed symptoms of having been subjected to unusual exertion. The supreme court accordingly affirmed the award in favor of the widow.—*Schneider v. F. & C. Haerter (N. J.)*, 197 A. 281.

Society Proceedings

COMING MEETINGS

- American Society of Tropical Medicine, Oklahoma City, Nov. 15-18.
Dr. E. Harold Hinman, Wilson Dam, Ala., Secretary.
American Student Health Association, New York, Dec. 29-30. Dr. Ruth E. Boynton, Students Health Service, University of Minnesota, Minneapolis, Secretary.
Pacific Coast Society of Obstetrics and Gynecology, Los Angeles, Nov. 30-Dec. 3. Dr. T. Floyd Bell, 400 29th St., Oakland, Calif., Secretary.
Radiological Society of North America, Pittsburgh, Nov. 28-Dec. 2. Dr. Donald S. Childs, 607 Medical Arts Bldg., Syracuse, N. Y., Secretary.
Society of American Bacteriologists, New Haven, Conn., Dec. 28-30. Dr. I. L. Baldwin, Agricultural Hall, University of Wisconsin, Madison, Wis., Secretary.
Southern Medical Association, Oklahoma City, Nov. 15-18. Mr. C. P. Loranz, Empire Bldg., Birmingham, Ala., Secretary.
Southern Surgical Association, White Sulphur Springs, W. Va., Dec. 6-8. Dr. Alton Ochsner, 1430 Tulane Ave., New Orleans, Secretary.
Western Surgical Association, Omaha, Dec. 2-5. Dr. Albert H. Montgomery, 122 South Michigan Blvd., Chicago, Secretary.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1928 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but may be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American Journal of Cancer, New York

84: 1-168 (Sept.) 1938

- Observations on Chorionepithelioma Testis: Record of Case. S. McDonald Jr., Birmingham, England.—p. 1.
Carcinoma of Kidney in Leopard Frog: Occurrence and Significance of Metastasis. B. Lucké, Philadelphia.—p. 15.
Leiomyoma of Oral Cavity. A. P. Stout, New York.—p. 31.
Carcinogenic Activity, Structure and Chemical Reactivity of Polynuclear Aromatic Hydrocarbons. L. F. Fieser, Cambridge, Mass.—p. 37.

American Journal of Clinical Pathology, Baltimore

8: 471-596 (Sept.) 1938

- *Early Diagnosis of Acute and Latent Plumbism. F. L. Smith 2d, T. K. Rathmell and G. E. Marcell, Philadelphia.—p. 471.
Monocytic Leukemia, with Analysis of Cell Characteristics by Supravital and Fixed Staining Technics. Regena Cook Beck, Richmond, Va.—p. 509.
Lymphile Complement in the Kolmer Complement Fixation Test for Syphilis. J. A. Kolmer, Carola E. Richter and Elsa R. Lynch, Philadelphia.—p. 522.
Flocculate Induced Antibodies and Syphilis Immunity in Rabbits. F. Rytz, Minneapolis.—p. 529.
*Serum Cholesterol Fluctuations During the Menstrual Cycle. F. M. Offenkrantz, with cooperation of Anne M. Staniel, Newark, N. J.—p. 536.
Histologic Study of Endometrium During Pregnancy. A. C. Broders and J. R. McDonald, Rochester, Minn.—p. 547.
Primary Carcinoma of Hepatic Ducts: Case Report. L. H. Snyder, Washington, D. C.—p. 563.
Leukemia in the Newborn, with Death at Birth from Traumatic Rupture of Spleen. B. W. Rhamy, Fort Wayne, Ind.—p. 567.
Pulmonary Sclerosis. R. J. Jermstad, Washington, D. C.—p. 573.

Early Diagnosis of Plumbism.—According to Smith and his associates, a differential diagnosis of lead poisoning can be accomplished by an accurate determination of lead in the serum, cells and fibrin fraction of the blood when taken into consideration with the total amount of lead in the whole blood. It is possible by this procedure to make a differentiation between acute, chronic and mild lead poisoning as well as to differentiate between mild lead toxemia and such pathologic conditions as gastro-enteritis, hypercalcemia, food poisoning, sun and x-ray burns or colics from other causes. The therapeutic use of lead can be controlled by this procedure, since deleading treatment may be instigated before an acute lead crisis develops. Results of 0.001 mg. of lead or less in 10 Gm. of serum, cells and fibrin or whole blood may be in error and should be considered qualitatively rather than quantitatively. Such a consideration does not change the interpretations, as the important factor is the appearance and disappearance of pathologic lead in the serum fraction of the blood. The essential difference in the manner in which the analysis of the blood of healthy persons differs from definite clinical cases of acute lead poisoning and periods of exacerbation in chronic lead poisoning lies in the appearance of lead in the serum fraction of the blood, since approximately 34 per cent of these cases show a whole blood content of less than 0.01 mg. of lead in 10 Gm. of blood and 18 per cent have a whole blood content bordering on the normal range of healthy persons. In thirty-four cases of latent and early acute phases of chronic plumbism there was a definite appearance of lead in the serum fraction of the blood in all the cases although the lead content of the whole blood in 68 per cent was less than 0.01 mg. in 10 Gm. and 44 per cent fell within the limits of the range established by healthy normal persons and patients with disorders other than plumbism. In inactive chronic plumbism the serum is normal but there is usually a definite increase in the lead content of the whole blood over that of the control group. However, a definite diagnosis may be established in

borderline cases by placing the patient on acid therapy as practiced in deleading, when an increase in the serum fraction and generally in the whole blood will occur. The clinical and physiologic course of lead intoxication through its quiescent periods as well as those of acute and subacute exacerbation may be followed by means of the analysis of the serum fraction and the whole blood for lead, and a prognosis established. Since it requires 10 Gm. of blood to make a determination for lead by the diphenylthiocarbazone method, the clinical procedure followed in cases complicated by the presence of malignant growths or blood dyscrasia is first to make an analysis of the lead content of the serum, cells and fibrin fraction and whole blood, then follow the trend of the intoxication by means of daily shiftograms and hemograms, and make additional blood analyses when they are hemographically or clinically indicated. However, in uncomplicated cases an analysis is made every second or third day. By such a procedure it is found possible to differentiate between symptoms caused by mild lead poisoning and those which result from pathologic conditions. A range of lead values for the healthy normal person is found to be nil in 10 Gm. of blood serum, from 0.002 to 0.011 mg. in 10 Gm. of cells and fibrin fraction and from 0.001 to 0.005 mg. in 10 Gm. of whole blood. This range was independent of sex, age, climatic changes, daily fatigue, violent exercise, meals, menstruation and ovulation.

Serum Cholesterol During Menstrual Cycle.—Offenkrantz presents data for each of a total of sixteen monthly cycles in sixteen young, healthy and regularly menstruating women. About eight determinations in a cycle were performed. The following facts were observed: 1. There is a sharp elevation of the total serum cholesterol at the end of the bleeding phase, associated with a slightly lowered percentage of free cholesterol. 2. There is a lowered total serum cholesterol at the onset of the menses. The percentage of free cholesterol is higher at this time than at its termination. 3. The intermediary cholesterol levels show a tendency to rise to the middle of the cycle and then fall off toward the new cycle. 4. Although there were wide fluctuations for each subject, no determination was outside the values previously found in other series on normal subjects. 5. There appear to be definite planes (i. e. higher, lower or intermediate levels) along which all the total cholesterol values for any subject will vary. These planes are held to be determined, in part, by the constitutional reaction type of the subject. 6. The narrow limits of fluctuation of the percentage of free cholesterol indicate the importance and stability of this factor. This variation is from 22.09 to 32.9 per cent of the total cholesterol. The meaning of this variation of cholesterol values with regard to the menstrual cycle is discussed.

American Journal of Diseases of Children, Chicago

56: 483-722 (Sept.) 1938

- *Intravenous Injection of Hypotonic Salt Solution Containing Sulfanilamide for Streptococci Meningitis. G. M. Retan, Syracuse, N. Y.—p. 483.
Effect of Milk Supplement on Physical Status of Institutional Children: II. Ossification of Bones of the Wrist. Vera MacNair, Rock Hill, S. C., and Lydia J. Roberts, Chicago.—p. 494.
Sedimentation Rate in Nutritional Anemia of Infants and Children: Its Response to Treatment with Iron (Ferrous Sulfate). C. H. Smith, New York.—p. 510.
Erythrocytes and Hemoglobin of Blood in Infancy and in Childhood: II. Variability in Number, Size and Hemoglobin Content of Erythrocytes During the First Five Years of Life. G. M. Guest, Estelle W. Brown and Mary Wing, Cincinnati.—p. 529.
Human Passive Transfer Antibody: III. Serial Titrations on Treated and Untreated Patients with Hay Fever. W. M. Schmidt and V. W. Lippard, New York.—p. 550.
*Minimal Vitamin C Requirements of Artificially Fed Infants: Study of 427 Children Under Controlled Dietary Regimen. B. M. Hamill, L. Reynolds, M. W. Poole and Icie G. Macy, Detroit.—p. 561.
*Comparative Study of Tuberculin Patch Test and Mantoux Intracutaneous Test. H. Vollmer, New York, and Esther W. Goldberger, Staten Island, N. Y.—p. 584.
Talmudic Contribution to the History of Diptheria. A. Bernstein, San Francisco.—p. 612.
Carcinoma of Thyroid Gland in Children: Report of Case Associated with Multiple Anomalies of Development, with Studies of Basal Metabolism, Serum Cholesterol and Creatine Excretion After Thyroidectomy. A. G. Langmann and Hilde Bruch, New York.—p. 616.

Saline Solution and Sulfanilamide in Meningitis.—In experiments on monkeys, planned to determine whether giving sulfanilamide intravenously has the advantage of increasing the concentration of the drug in the cerebrospinal fluid, Retan observed that when physiologic solution of sodium chloride

containing sulfanilamide is given to monkeys intravenously the concentrations of sulfanilamide are greater in the blood than in the cerebrospinal fluid. When a hypotonic solution of sodium chloride containing sulfanilamide is injected intravenously, the concentrations during the first injection are the same as with the physiologic solution. However, if the injection of a hypotonic solution is repeated on the second day there occurs a shift to a higher percentage of sulfanilamide in the cerebrospinal fluid than is contained in the blood. A similar shift to higher concentrations in the cerebrospinal fluid than in the blood can be produced by giving the drug by mouth in solution or in capsules prior to the intravenous injection of a hypotonic solution of sodium chloride. The shift depends on the presence of sulfanilamide in the tissues of the body and the intravenous introduction of a hypotonic solution of sodium chloride containing sulfanilamide. The author is not in a position to know what result he should have obtained in his case of hemolytic streptococcus meningitis had he given sulfanilamide by mouth and by subcutaneous injection without using injections of hypotonic solution of sodium chloride containing sulfanilamide. However, every one who saw the patient was impressed by the prompt subjective and objective improvement shown within an hour of the beginning of each intravenous injection. He believes that this method of treatment is based on sound theoretical grounds. It would seem that the doses of sulfanilamide used in the intravenous solution (from 6 to 10 Gm. in twenty-four hours) were unnecessarily large. In his next case he plans to give about half as much sulfanilamide in the hypotonic solution. However, there were no harmful results. An alkaline powder of calcium carbonate and sodium bicarbonate was given at intervals of four hours. The rate of injection most successfully used is 10 cc. of solution each hour per pound of body weight. A 0.375 per cent solution has been found to be most effective. Treatment for five hours with rest intervals of several hours between treatments is advised. Cerebrospinal fluid is released from the lumbar puncture needle during the intravenous injection for the purpose of relieving increased intracranial pressure. If the fluid is under considerable pressure and is spurting from the needle, it is wise to drain from 5 to 10 cc. during half an hour. If the fluid is dripping rapidly, less than this amount should be drained. If the fluid emerges from the needle by a slow drop, the stylet should be replaced at once without draining any fluid. The drainage of too great an amount of cerebrospinal fluid during the intravenous injection of a hypotonic solution of sodium chloride can result in cerebellar herniation.

Minimal Vitamin C Requirements.—Hamil and his co-workers studied 427 infants, comprising a cross section of the indigent and near indigent class of Detroit, during their first year of life. Of these 80 per cent were under observation for nine months or longer. The children were in their home environment, and the investigation was closely controlled. Almost 10 mg. of vitamin C was made available to each infant daily by the addition of powdered lemon juice to their formulas. It appeared that the minimal protective dose of vitamin C for the average healthy infant is about 10 mg. daily. Comprehensive examinations of each infant were made monthly or more often. From the data on the 427 infants observed it appears that the condition which has usually been considered latent scurvy is actually definite mild scurvy. It seems that scurvy is a definite pathologic entity but does not become evident or retard development until the absence of the specific physiologic functions of the vitamin is manifest. During the course of the study twenty-one infants had mild scurvy. During the time mild scurvy was present the rates of gain in weight and height were retarded but development in sitting, standing, creeping, walking and talking was not. From the results it appears that an infection predisposes to mild scurvy but is not a concomitant symptom of the condition. Lowering of the hemoglobin level does not appear to be a symptom of mild scurvy nor does it predispose to the development of this disease.

Tuberculin Patch and Mantoux Tests.—Of 169 children with active tuberculosis whom Vollmer and Goldberger tested only one of those who reacted positively to the Mantoux test with the stronger solution of purified protein derivative failed to react positively to the tuberculin patch test. Among 118 children admitted in a routine manner to the pediatric service

of the Mount Sinai Hospital with various diseases the Mantoux test, even with 1 mg. of old tuberculin, did not reveal a single case of tuberculous infection which was not already discovered by the tuberculin patch test.

Am. J. Roentgenol. & Rad. Therapy, Springfield, Ill. 40: 325-484 (Sept.) 1938. Partial Index

- Practical Importance of Mechanics in Digestion. A. E. Barclay, Oxford, England.—p. 325.
Experimental Studies on Gastric Physiology in Man: IV. Influence of Osmotic Pressure Changes of Salt and Sugar Solutions on Pyloric Action and Gastric Emptying in Normal and Operated Stomach. J. Gershon-Cohen, H. Shay and S. S. Fels, Philadelphia.—p. 335.
Ventriculographic Localization of Intracranial Tumors: II. Tumors of Aqueduct, Pons and Cerebellopontile Angle. V. C. Johnson, C. F. List, Ann Arbor, Mich.—p. 348.
Enlarged Glomus Defect Contralateral to the Side of Ventricular Puncture: Its Occurrence Due to Cysts of Glomus. M. H. Poppel, New York.—p. 357.
Shape of the Female Pelvis and Its Clinical Significance: Further Roentgen Studies. L. H. Garland, San Francisco.—p. 359.
Roentgenologic Diagnosis of Perinephric Abscess and Perinephritis. A. E. Goldstein and M. Ostro, Baltimore.—p. 371.
Roentgen Diagnosis of Reducible Hernia. Carye-Belle Henle, Newark, N. J.—p. 392.
Visualization of the Aorta by the Method of Roentgenographic Overpenetration. B. S. Epstein, Brooklyn.—p. 396.
End Results of Irradiation of Thymus Gland in Twenty-Seven Normal Infants and Children. C. G. Kerley, New York.—p. 416.
Some Effects of Radiation on Oil. W. Stenstrom and I. Vigness, Minneapolis.—p. 427.

Shape of the Female Pelvis and Its Clinical Significance.—On a morphologic or architectural basis Garland classifies female pelvis into four main types: gynecoid, android, anthropoid and platypelloid. In a group of 150 unselected primiparas the incidence of these types was found to be gynecoid 51, android 21, anthropoid 18 and platypelloid 10 per cent. Approximately 79 per cent were pure types and 21 per cent mixed types. The size of the pelvic inlet, the width of the subpubic angle and the shape of certain other anatomic features were carefully measured. These data are of value in arriving at the correct x-ray interpretation but are independently variable within wide limits. The inclination of the pelvic inlet relative to the horizontal, with the patient recumbent, was studied and it was found that in the average case it is approximately 20 degrees (not 42 degrees as reported in the literature). The clinical significance of this observation in connection with certain classic obstetric maneuvers is obvious. With reasonable care the shape of the female pelvis can be readily diagnosed by a set of three roentgenograms, and, especially in the android type, a potentially difficult labor can be forecast in patients whose obstetric measurements by ordinary clinical methods appear normal.

Annals of Internal Medicine, Lancaster, Pa. 12: 285-428 (Sept.) 1938

- The Heart in Pulmonary Tuberculosis: Electrocardiographic Consideration. W. R. Leverton, San Fernando, Calif.—p. 285.
Common Gastrointestinal Emergencies and Their Medical Aspects. G. B. Eusterman, Rochester, Minn.—p. 306.
Clinical Observations, Complications and Treatment of Acute Upper Respiratory Tract Infections. A. V. Bock, Cambridge, Mass.—p. 317.
Constitutional Factors in Arthritis, with Special Reference to Incidence and Role of Allergic Diseases. R. T. Pottenger, Pasadena, Calif.—p. 323.
Affective Disorders in Medical Practice. T. P. Sprunt, Baltimore.—p. 334.
Studies on Life Histories of Patients with Chronic Ulcerative Colitis (Thrombo-Ulcerative Colitis), with Some Suggestions for Treatment. J. A. Bergen, R. J. Jackman and J. G. Kerr, Rochester, Minn.—p. 339.
Quinine and Atabrine: A Comparison. O. T. Brosius, Santa Marta, Colombia.—p. 353.
Coronary Artery Disease and Angina Pectoris: Present Status with Review of Some of the Recent Literature. I. C. Brill, Portland, Ore.—p. 365.
The Mechanism of Heat Loss and Temperature Regulation. E. F. Du Bois, New York.—p. 388.

Infections of Respiratory Tract.—Bock discusses the care of 1,667 cases of acute infection of the respiratory tract treated by himself and his associates from September 1935 to March 1938. The subjects were undergraduate and graduate students at Harvard, the principal age range being from 17 to 25 years. The main purpose of his discussion is to make a plea for simple treatment, the fruits of which are perhaps best indicated by the relatively small list of complications (twenty-nine cases of otitis media, one of mastoiditis, two surgically drained antrums, one peritonsillar abscess and fifty-two of pneumonia) of all sorts

occurring in this series. Common sense treatment of acute infections of the upper part of the respiratory tract, including the common cold, with or without fever, requires bed care. Whatever the specific etiologic factors may be, it is clear to the author that fatigue of body and mind in adult patients is a factor in the precipitation of these infections not generally recognized. The main principle of treatment should be rest. Energetic local treatment produces irritation of the nasopharyngeal membranes, often prolonging the course. Salicylates and codeine are used for comfort. Laxatives are not usually prescribed. Control of temperature, humidity and dust would add greatly to the effectiveness of treatment. Prevention of infections of the upper part of the respiratory tract by vaccines has little to support it. Lacking specific means of therapy, the greatest advance on the problem at the moment would be made if the physician taught himself and his patients how to live within his and their physical resources, and especially within those of one's central nervous system. Such influences as chilling of the body, weather changes, irritative substances in the atmosphere and contagion must be taken into account; but granting these, under ordinary circumstances, the part played by the tension of living must be recognized more generally in solving the problem.

Chronic Ulcerative Colitis.—During the years 1925 to 1931 inclusive Bergen and his colleagues observed seventy-three patients who had tuberculous ileocolitis at the Mayo Clinic, approximately 500 who had amebic colitis, 129 who had ulcerative colitis of undetermined etiology and 871 who had thrombo-ulcerative colitis (of bacterial origin). A statistical study of the records of the 871 patients who had thrombo-ulcerative colitis, followed from seven to fourteen years after the first observation, shows that the predisposing factors and those affecting relapses of the disease are: infections of the upper part of the respiratory tract, disease of childhood, dietary indiscretion, physical and mental fatigue, rectal or abdominal surgery, trauma, drastic catharsis, foci of infection with sepsis, exposure, dysentery epidemics and pregnancy. This disease may begin in an insidious manner. Again it may come on suddenly as a violent diarrhea without toxic symptoms or it may start in a fulminating fashion associated with marked toxemia, fever and all the concomitants of a severe septic process. The major complications and sequelae of thrombo-ulcerative colitis include polyposis, stricture, perianal abscess-fistula, arthritis, erythema nodosum, pyoderma gangrenosa, perforation, hepatic abscess, carcinoma, phlebitis, iritis, deafness, splenomegaly, nephritis, psychosis, massive hemorrhage, endocarditis and renal stones. There is no special time of year in which the disease begins, but more of the cases had their onset in January, February or July than in the other months of the year. The progress of the invasion from the rectum toward the cecum is indicative of its destructive nature. The mortality (at the time of inquiry 19.3 and 12.9 per cent, male and female, respectively) associated with this destructive infection emphasizes its serious nature. Surgical intervention in this disease should be limited to complications and sequelae. Some of these demand wisely chosen surgical measures, both from the standpoint of the time of their application and from that of the lesion present. A person with thrombo-ulcerative colitis presents a poor surgical risk if a surgical attempt must be made to relieve another intercurrent abdominal pathologic condition. Complete relief of all symptoms and signs of intestinal pathologic change occur frequently enough to make it urgent that a well ordered regimen be followed without deviation by these patients for months and years.

Annals of Medical History, New York

10: 369-462 (Sept.) 1938

- Santorio Santorio. R. H. Major, Kansas City, Kan.—p. 369.
Captured Medical Men and Army Hospitals of the American Revolution. J. E. Gibson, Philadelphia.—p. 382.
Sketches of the Life and Interests of Sir Hans Sloane: Naturalist, Physician, Collector and Benefactor. B. Chance, Philadelphia.—p. 390.
L'Hôpital Saint-Louis: Brief Biographic Sketch of Its Early Teachers and Their Influence on American Dermatology. P. E. Bechel, New York.—p. 405.
Eighteenth Century Obstetrics and Obstetricians in the United States. E. M. Jameson, Saranac Lake, N. Y.—p. 413.
Maimonides' Prayer. S. R. Kagan, Roxbury, Mass.—p. 429.
Some Remarks on Keats and His Friends. R. Armstrong-Jones, London, England.—p. 433.
Alexander Porfirivich Borodin: Physician, Chemist and Composer. F. W. Sunderman, Philadelphia.—p. 445.

Archives of Internal Medicine, Chicago

62: 547-722 (Oct.) 1938

- *Action of Digitalis in Compensated Heart Disease. H. J. Stewart, N. F. Crane, J. E. Deitrick and W. P. Thompson, New York.—p. 547.
Action of Digitalis in Uncompensated Heart Disease. H. J. Stewart, J. E. Deitrick, N. F. Crane and C. H. Wheeler, New York.—p. 569.
Clinical Studies of Respiration: VII. Additional Observations Concerning Validity of Results Obtained with Body Plethysmograph. J. A. Greene, L. W. Swanson and R. H. Heeren, Iowa City.—p. 593.
Pneumonia Complicated by Acute Pneumococcal Hemorrhagic Ulcerative Gastro-Enteritis (Dieulafoy's Erosion): Report of Two Cases. C. H. Sanford, J. D. Hughes and J. Weems, Memphis, Tenn.—p. 597.
Diabetes Insipidus as Sign of Metastatic Involvement of Supra-Opticohypophyseal System. M. Bernstein, M. T. Moore and D. B. Fishbach, Philadelphia.—p. 604.
*Chemical Factors Concerned in Formation of Gallstones. R. E. Dolkart, K. K. Jones and C. F. G. Brown, Chicago.—p. 618.
Primary Carcinoma of Lung: Clinical and Pathologic Study of 100 Cases. S. Koletsky, Cleveland.—p. 636.
Gastro-Enterology: Review of the Literature from January 1937 to June 1938. C. M. Jones, T. V. Urmy, E. B. Benedict, M. H. Clifford and B. V. White, Boston.—p. 652.

Digitalis in Compensated Cardiac Disease.—Stewart and his co-workers gave from 1.6 to 1.8 Gm. of digitalis within twenty-four hours to thirteen patients suffering from rheumatic cardiac disease and to four others with arteriosclerotic, hypertensive or syphilitic cardiac disease. There was compensation, and a normal sinus mechanism was exhibited. In all cases the T wave and the RT segment of the electrocardiogram showed the changes characteristic of a digitalis effect. Seven patients showed a decrease in cardiac output and a decrease in cardiac size, four patients showed an increase in cardiac output and a decrease in cardiac size, and six patients showed no change in cardiac output and in cardiac size. In short, in some instances when the heart was made smaller the cardiac output increased, and in others it decreased. In the former cases the heart behaved like a failing heart and in the latter cases like a normal one. The results in five patients exhibiting auricular fibrillation were not different from those encountered in those with normal sinus rhythm—a decrease in cardiac size was associated with a decrease in cardiac output, and an unchanged cardiac size was associated with an unchanged cardiac output. A few observations on patients with cardiac disease due to other etiologic factors showed that the phenomena of digitalis are not confined to those with rheumatic involvement. There is one phenomenon which is common to all groups: the giving of digitalis increases the work accomplished by the heart per beat, whether its action is to increase or to decrease the output or to leave it unaltered and whether the rhythm is regular or that of auricular fibrillation. As a consequence, work becomes more nearly appropriate for the size of the organ. Some basis is afforded Christian's suggestion of giving digitalis to the patient suffering from organic cardiac disease even though he shows no significant failure. A decrease in cardiac output which follows the giving of digitalis to human beings (normal and those having organic cardiac disease without congestive cardiac failure) is not a consequence of diminished venous return but a consequence of a decrease in the size of the heart due to the action of digitalis.

Chemical Factors in the Formation of Gallstones.—According to Dolkart and his associates, in all the various bile salt preparations used in the experiments the sodium salt of pure cholic acid proved to have the greatest cholesterol-solvent capacity, with sodium taurocholate, sodium desoxycholate and sodium glycocholate, in the order named, next in activity. There appears to be an optimal concentration for some of the preparations used. Changes in the structure of the bile acid molecule have a marked effect on the ability of the particular acid to hold cholesterol in solution. Conjugation with aminoacetic acid or taurine somewhat decreases this ability. The oxidation of desoxycholic acid to the keto form resulted in a marked loss of solvent capacity. Mixed ketocholanic acid showed moderate ability to hold cholesterol in solution, and it appears that some additional substance—possibly chenodesoxycholic or lithocholic acid—is present. The authors' results demonstrate that bile salts are not the most essential substances for maintaining cholesterol in solution in the bile. In equivalent concentrations the fatty acids were far more active as cholesterol solvents than were the bile acids. The studies of the cholesterol-solvent capacity of fractions of bile showed that whether or not the animal belonged to a species which forms gallstones, if the bile

was solvent for cholesterol, the solvent capacity could be isolated in the saponifiable or fatty acid fraction. There was a considerable decrease in the amount of this saponifiable fraction in relation to the cholesterol content of the bile in those animals which form gallstones, as compared with the amount in those which never form gallstones. Whether the fatty acids as they occur in the bile function independently in maintaining the non-saponifiable material in solution in the bile or whether they act in combination with the bile acids, as suggested by Wieland and Sorge and Verzar, cannot at present be determined. However, more attention should be given the role of the fatty acids in the production of gallstones.

Archives of Pathology, Chicago

26: 765-922 (Oct.) 1938

- Cerebral Lesions in Hypoglycemia: II. Some Possibilities of Irreversible Damage from Insulin Shock. A. B. Baker, Minneapolis.—p. 765.
Experimental Production of Tumors in the Brains of White Rats. A. Weil, Chicago.—p. 777.
Medulloblasts of the Infant Brain. C. R. Tuthill, Staten Island, N. Y.—p. 791.
Cytologic Changes in Skin of Mice During Application of Carcinogenic Agents. R. C. Page, Rochester, Minn.—p. 800.
Latent Period in Growth of Spontaneous Mammary Carcinoma in Female Mice of the A Strain. L. C. Strong, New Haven, Conn.—p. 814.
Cardiovascular and Other Lesions in Calves Fed Diets Low in Magnesium. L. A. Moore, E. T. Hallman and L. B. Sholl, East Lansing, Mich.—p. 820.
*Frequency with Which Syphilitic Lesions Are Encountered in Postmortem Examinations. E. T. Bell, Minneapolis.—p. 839.
Pigmented Adenoma of Adrenal. Margaret R. Baker, Akron, Ohio.—p. 845.
Major Duodenal Papilla: Variations of Pathologic Interest and Lesions of Mucosa. A. H. Baggenstoss, Rochester, Minn.—p. 853.

Frequency of Syphilitic Lesions in Postmortem Examinations.—Bell in a survey of 27,872 postmortem examinations found definite syphilitic lesions in 2.77 per cent, and in approximately 2.5 per cent syphilis was shown to be the major cause of death. About 3.38 per cent of stillborn infants were syphilitic, and congenital syphilis caused about 2.63 per cent of the deaths in infants less than 1 year of age. Congenital syphilis was a rare cause of death in infants more than 1 year of age. Syphilis was an infrequent cause of death in persons dying in the second and third decades of life. The maximal mortality from this cause occurred in persons in the fourth, fifth and sixth decades of life. Acquired syphilis, in its lethal forms at least, was about twice as frequent in men as in women. The major forms of lethal syphilis were syphilitic aortitis and neurosyphilis, and the age distribution peaks of these two forms were at 45 and 35 years of age, respectively.

Arkansas Medical Society Journal, Fort Smith

35: 89-104 (Oct.) 1938

- Possibilities of Modern Chest Surgery. J. K. Donaldson, Little Rock.—p. 89.
Hyperparathyroidism: Case Report. W. F. Adams, Fort Smith.—p. 92.
Medical Care Plans. R. G. Leland, Chicago.—p. 96.

Endocrinology, Los Angeles

23: 263-392 (Sept.) 1938

- Innervation of Hypophysis. A. T. Rasmussen, Minneapolis.—p. 263.
Changes in Hypophysis and Ovaries of Rats Chronically Treated with an Anterior Pituitary Extract. J. B. Collip, H. Selye and J. E. Williamson, Montreal.—p. 279.
Hormone Studies with Ultracentrifuge: II. Concentration of Anterior Lobe and Pituitary-like Hormones with Ultracentrifuge. Aura E. Severinghaus, L. Levin and J. A. Chiles Jr., New York.—p. 285.
Effect of Hypophysectomy on Restoration of Liver Following Partial Hepatectomy in Rats. C. C. Franseen, A. M. Brues and R. L. Richards, Boston.—p. 292.
Reliability of Present Methods for Characterizing Two Gonadotropic Hormones, Follicle Stimulator and Luteinizer. F. J. Saunders and H. H. Cole, Davis, Calif.—p. 302.
Diabetic Traits in Strain of Rats. Versa V. Cole and B. K. Harned, Philadelphia.—p. 318.
Endocrine Factors Influencing Tumor Development: Effect of Prolan on Marsh-Buffalo Adenocarcinoma. F. Bischoff and M. Louisa Long, Santa Barbara, Calif.—p. 327.
Blood Potassium and Suprarenal Glands. A. D. Marenzi, Buenos Aires, Argentina.—p. 330.
Effect of Testosterone Propionate on X Zone of Mouse Adrenal. W. F. Starkey and E. C. H. Schmidt Jr., Pittsburgh.—p. 339.
Effects of Certain Gonad and Gonadotropic Hormones on Gestation Period of the Rat. C. A. Bunde, Madison, Wis.—p. 345.
Induction of Brooding Behavior in the Jewel Fish. G. K. Noble, K. F. Kumpf and V. N. Billings, New York.—p. 353.

Indiana State Medical Assn. Journal, Indianapolis

31: 537-592 (Oct.) 1938

- Causes of Blindness Among the Children at the Indiana State School for the Blind. R. Masters, Indianapolis.—p. 537.
The State and the Blind. Jean R. Kettler and J. M. McCaslin, Indianapolis.—p. 539.
Causes of Blindness in Adults. C. W. Rutherford, Indianapolis.—p. 543.
Blindness in Adults Due to Injury. C. P. Clark, Indianapolis.—p. 547.
Common Causes of Eye Injuries in Children: Ways to Avoid Them. H. Row, Indianapolis.—p. 549.
Conservation of Vision. J. V. Cassady, South Bend.—p. 552.
A Fracture Traction Apparatus for the General Practitioner. W. M. Loehr, Versailles.—p. 554.
Electrosurgical Excisional Biopsy. E. N. Kime, Indianapolis.—p. 556.
A Suggested Plan for Consideration on the Problem of Health Security. N. K. Forster, Hammond.—p. 560.
Foreign Body in the Vagina: Case Report. E. T. Leslie, Evansville.—p. 564.

Journal of Allergy, St. Louis

9: 535-650 (Sept.) 1938

- *Specific Diagnosis and Treatment of Poison Ivy (Rhus Toxicodendron) Dermatitis. A. H. W. Caulfield, Toronto.—p. 535.
Active Immunization of Allergic Individuals Against Tetanus by Means of Tetanus Toxoid, Alum Precipitated Refined. H. Gold, Chester, Pa.—p. 545.
*Total, Free and Ester Cholesterol Content of Serum in Hay Fever and in Asthma. M. Bruger, F. E. Sammis, W. C. Spain and S. Member, New York.—p. 551.
Tobacco Allergy and Thrombo-Angiitis Obliterans. F. H. Westcott and J. S. Wright, New York.—p. 555.
Emotional Component of Bronchial Asthma. C. H. Eyermann, St. Louis.—p. 565.
Intrapulmonary Inhalation of Benzedrine: Preliminary Report of Some Clinical Effects. O. Swineford Jr., University, Va.—p. 572.
Urticaria of Bacterial Origin. O. C. Hansen-Prüss, Durham, N. C.—p. 577.
Urticaria of Serum Sickness Type: Report of Five Cases. G. L. Waldbott and M. S. Ascher, Detroit.—p. 584.
Retention of Lipidol in Lungs: Two Case Reports. G. Flamm, New York.—p. 593.
Soybean Sensitivity: Case Report. H. B. Wightman, New Rochelle, N. Y.—p. 601.
Asthma Due to Sensitization to a Mushroom Fly (Aphiochaeta Agarici). R. A. Kern, Philadelphia.—p. 604.
Beet Pollen and Beet Seed Dust Causing Hay Fever and Asthma. L. O. Dutton, El Paso, Texas.—p. 607.
Sensitization to Jute. F. A. Stevens and L. Jordani, New York.—p. 610.

Poison Ivy Dermatitis.—The extract from the poison ivy plant that Caulfield has termed "rhologin," suitably diluted for patch testing, has been found of value in the differential diagnosis of dermatitis regarded as possibly due to contact with poison ivy. The intramuscular injection of this extract in increasing amounts actively influences the severity and duration of an attack of poison ivy dermatitis. Following an adequate series of intramuscular injections of this extract, twenty-three persons susceptible to poison ivy dermatitis have shown a greatly reduced (with a questionable reservation in one case) or even a negative quantitative patch test. Practical clinical results, based on reexposure to the same environment, have confirmed the theoretical conclusion that a satisfactorily reduced quantitative patch test coincides with clinical immunity to ordinary contact with this plant. Dosage and reactions are reciprocal; the greater the degree of sensitivity, the greater the number of injections (from eight to twenty-six injections have been given) which must be given if one is to avoid uncomfortable reactions. The most frequently encountered reaction has been a dermatitis about the site of the injection. At least forty-six persons have been patch tested with rhologin. Twenty-five of these patients were referred with the diagnosis of poison ivy dermatitis. Nine of these gave either a 2, 3 or 4 plus reaction, thus fully confirming the causation. In seven the patch test was negative. With these seven there would seem to be no doubt that the dermatitis was not caused by poison ivy. In the remaining nine cases a 1 plus reaction was obtained. In seven of these the attack was relatively mild and of short duration, so that the clinical diagnosis would seem to be in accord with the results of the tests.

Serum Cholesterol in Hay Fever and Asthma.—Bruger and his co-workers determined the cholesterol partition of the serum before and during treatment of 121 patients when they were free from typical attacks of bronchial asthma and seasonal hay fever. The average total cholesterol for the forty-nine patients with hay fever who were treated was 222 ± 67 mg. per

hundred cubic centimeters of serum as compared to the values observed by Sperry in normal adults of 210 ± 50 mg. The average amount of free cholesterol in total cholesterol was 34 ± 8.3 mg. per hundred cubic centimeters, which is somewhat higher than the average normal values. In the treated asthma group (fifty patients) the average total cholesterol was 199 ± 50 mg. per hundred cubic centimeters; the average amount of free cholesterol in total cholesterol was 32.4 ± 7.5 mg. per hundred cubic centimeters. Here again the proportion of free in total cholesterol was somewhat higher than the normal values. In the twenty-two patients with untreated hay fever and asthma (eleven in each group) the average total cholesterol was 198 and 197 mg., and the average free cholesterol in total cholesterol was 29 and 31 mg., respectively. The degree of variation from the treated allergic groups is not noteworthy. Although the average total cholesterol in the treated hay fever group is greater than the average normal figure and in the treated asthma group somewhat lower, the variation from normal is not striking, lacking significance from a statistical point of view.

Journal of Lab. and Clinical Medicine, St. Louis

23: 1223-1332 (Sept.) 1938

- Salmonella Suipestifer Infection: Report of Case. D. B. Cole and W. L. Nalls, Richmond, Va.—p. 1223.
- *Ascorbic Acid in Blood and Urine After Intravenous Injection of Sodium Ascorbate: Clinical Test for Determining Vitamin C Deficiency. E. S. G. Barron, H. J. Brumm and G. F. Dick, Chicago.—p. 1226.
- Notes on Nature and Uses of Protamines in Treatment of Diabetes: Experimental Study of Effect of Protamine Insulinate on Estrous Cycle of White Rats. J. R. Williams, Rochester, N. Y.—p. 1237.
- Experimental and Clinical Considerations of Actions of Camphorhetrazol, Metrazol and of Schizophrenic Psychoses. D. E. Jackson and Helen L. Jackson, Cincinnati.—p. 1240.
- Biochemical and Morphologic Methods for Isolation and Identification of Yeastlike Fungi. C. C. Croft and L. A. Black, College Park, Md.—p. 1248.
- *Yeastlike Fungi Isolated from Normal Skins. C. C. Croft and L. A. Black, College Park, Md.—p. 1259.
- Glutathione Content of Blood During the Puerperium. J. F. Cadden, New York.—p. 1266.
- Determination of Para-Aminobenzenesulfonamide: Micromethod. E. A. MacLachlan, B. W. Carey Jr. and A. M. Butler, Boston.—p. 1273.
- Observations on Neufeld Reaction (Quellung Test) Following Desiccation of Pneumococcus Preparations. H. R. Brown, Rochester, N. Y.—p. 1277.
- Errors in Erythrocyte Counts Due to Hayem's Solution, Avoided with Gowers' Solution. Y. C. Ch'u, Shanghai, China, and C. E. Forkner, New York.—p. 1282.
- Note on Preparation of Urease Reagent for Wrenn's Method for Determination of Urea in Blood and Urine. D. B. Sabine, Yonkers, N. Y.—p. 1296.
- Lantern Slides of Photomicrographs in Color: Simplified Method. W. R. Jones, Seattle.—p. 1297.
- Simplified Method for Making Photographic Records of Petri Dish Cultures Without Camera. E. Maier, Venice, Fla.—p. 1299.
- Method for Protection of Microscopic Mounts for Mailing. H. P. Barret and Theresa Culp, Charlotte, N. C.—p. 1300.
- Improved Method of Examination of Spinal Fluid for Diagnosis of General Paresis. H. Hecht, Prague, Czechoslovakia.—p. 1301.
- Microchemical Method for Determination of Manganese by Oxidation with Potassium Persulfate: Critical Study of Persulfate Method. T. W. Ray, Milwaukee.—p. 1304.
- The Kahn Reactions of Sixty-Four Tularemia Patients. Elizabeth C. Brown and N. Nagle, St. Louis.—p. 1310.

Ascorbic Acid in Blood and Urine.—Barron and his associates determined the rate of disappearance from the blood and the urinary excretion of ascorbic acid after the injection of 10 mg. of sodium ascorbate per kilogram of body weight in sixty-three patients. The ascorbic acid content of the blood was estimated by centrifuging oxalated blood in a cold room (3 C.); 2 cc. of the plasma is added to a centrifuge tube containing 6 cc. of trichloroacetic-metaphosphoric acid mixture (1.2 Gm. of metaphosphoric acid ground in a mortar immediately before being dissolved in 40 cc. of a solution of 12.5 Gm. per cent of trichloroacetic acid), shaken together and centrifuged. The supernatant fluid (3 cc.) is titrated with the dilute dye (2 cc. of stock dye [25 mg. of 2,6-dichlorophenol indophenol dissolved in 50 cc. of warm distilled water and filtered] diluted to 25 cc. with distilled water) until a pink color, stable for half a minute, appears. In the urine specimens the ascorbic acid is titrated with the stock dye after the addition of 4 drops of the trichloroacetic-metaphosphoric acid mixture. For the twenty-four hour sample as well as the control twenty-four hour period sample the urine is collected in a bottle containing 25 cc. of five times normal sulfuric acid plus about 50 mg. of 8-hydroxy-

quinoline and kept in the ice box until the moment of the titration. The "three hour" and "eight hour" samples were titrated after acidification as soon as received. If toluene is added the urine may be kept for twenty-four hours at room temperature with no loss of ascorbic acid. There seems to be, in general, a relation between the content of ascorbic acid in the blood before the injection of ascorbic acid and the percentage of urinary excretion twenty-four hours after the injection; a urinary excretion of ascorbic acid of 10 per cent or less in twenty-four hours is evidence of vitamin C deficiency. Patients having less than 0.4 mg. of ascorbic acid per hundred cubic centimeters of blood showed, as a rule, a low rate of urinary excretion. Contrary to published reports there was no correlation between the content of ascorbic acid in the blood and the rate of its disappearance from the blood after the injection. A survey of the physiologic functions of ascorbic acid suggests that its deficiency may produce varied pathologic alterations other than scurvy. There were three patients with a high ascorbic acid content in the blood and a low urinary excretion. All of them had renal impairment. In the first case the ascorbic acid content of the blood was 2.09 mg. per hundred cubic centimeters and the urinary excretion only 47.4 per cent. In the second case the blood ascorbic acid was 1.75 mg. with a urinary excretion of 13.8 per cent; the patient had an arteriosclerotic cardiac disease associated with cardiac hypertrophy. The third case, with a blood ascorbic acid of 1.32 mg. and a urinary excretion of 18.2 per cent; was that of an adrenal tumor. If ascorbic acid deficiency is observed in Addison's disease (two cases cited) it must be a consequence of low vitamin intake or impaired renal function. It is quite possible that many symptoms observed in gastrointestinal disorders and designated as functional or neurotic are the consequence of hypovitaminosis due to the use of diets poor in vitamin content.

Yeastlike Fungi from Normal Skins.—From scrapings from the finger tips and nails of 100 persons, Croft and Black isolated twenty-nine cultures of yeastlike fungi from twenty-two of the persons tested. Persons whose hands were kept moist a large part of the time (kitchen workers, laboratory apparatus washers and housewives) showed a higher incidence to yeastlike fungi than those with drier hands. Twelve cultures were classified as being similar or closely related to *Monilia parapsilosis*, three as *Monilia nigra* and three an unidentified *Monilia* species. Four *Endomyces* species were isolated. These are the first organisms of this type known to be reported from normal skin. Two *Cryptococcus* species, one *Mycoderma* species, one *Schizosaccharomyces hominis* and three yeastlike fungi that could not be identified were also isolated. *Monilia albicans*, or any known pathogenic yeastlike fungus, was not isolated from the normal skins.

Journal of Pharmacology & Exper. Therap., Baltimore

64: 1-130 (Sept.) 1938

- Pharmacologic Studies on Diethane Hydrochloride. T. H. Rider with E. S. Cook, Cincinnati.—p. 1.
- Therapeutic Assay of Neoarsphenamine with *Trypanosoma Equiperdum*. C. A. Morrell, C. W. Chapman and M. G. Allmark, Ottawa, Ont.—p. 14.
- *Effect of Sodium Amytal, Sodium Barbital and Nembutal on Electrocardiogram. Roberta Hafkesbring and Winona MacCalmont, Philadelphia.—p. 43.
- Hypnotic Action of Certain Tertiary Butyl Aliphatic Amides. A. D. Bass, Nashville, Tenn.—p. 50.
- Placental Transmission of Selenium. B. B. Westfall, E. F. Stohltman and M. I. Smith, Washington, D. C.—p. 55.
- Bronchodilator Action of Magnesium and Its Antagonistic Action (Dilator Action) Against Pilocarpine, Histamine and Barium Chloride. V. G. Haurry, Philadelphia.—p. 58.
- Studies on Native Glucosides of *Digitalis Lanata*, with Particular Reference to Their Effects on Cardiac Efficiency and Their Toxicity. G. K. Moe and M. B. Visscher, Minneapolis.—p. 65.
- Electrocardiographic and Blood Pressure Changes Induced by Posterior Pituitary Extract (Pitoblobin V), and Influence of Ephedrine Thereupon. K. I. Melville, Montreal.—p. 86.
- Anesthesia and Liver Damage: II. Effect of Anesthesia on Blood Sugar, Liver Glycogen and Liver Fat. J. S. Ravdin, H. M. Vars, S. Goldschmidt and L. E. Klingensmith, Philadelphia.—p. 111.

Effect of Barbiturates on Electrocardiogram.—Hafkesbring and MacCalmont studied the effect of derivatives of barbituric acid on the electrocardiograms of dogs and cats before, during and after the administration of the drug. The only

cardiac effects of anesthetic doses of barbital, amytal and pentobarbital sodium were an increase in heart rate and a decrease in sinus arrhythmia. Electrocardiograms taken the day after the administration of these drugs showed complete recovery. There was no evidence to indicate the occurrence of cumulative effects or the development of a tolerance to the drugs used.

Kansas Medical Society Journal, Topeka

39: 369-412 (Sept.) 1938

- Primary Carcinoma of the Lung: Clinical Study of 160 Cases in Five Years. A. Arkin, Chicago.—p. 369.
Congenital Syphilis. D. N. Medearis, Kansas City.—p. 372.
Negative Phase of Typhoid Vaccination. M. Gerundo, Topeka.—p. 376.
Bilateral Streptococcal Empyema. G. B. Kent and K. C. Sawyer, Denver.—p. 379.
Postoperative Fecal Fistula: Report of Case. M. A. Walker and H. H. Hesser, Kansas City.—p. 382.
X-Ray Treatment of Erysiploid. M. A. Walker and L. G. Allen, Kansas City.—p. 383.
Use of Barbiturates in Surgery: II. M. A. Walker, G. R. Peters and P. E. Hiebert, Kansas City.—p. 383.

Missouri State Medical Assn. Journal, St. Louis

35: 385-423 (Oct.) 1938

- Obesity in the Adult. A. A. Werner and D. C. Weir, St. Louis.—p. 385.
Intermenstrual Pain. D. L. Sexton, St. Louis.—p. 388.
Fat Embolism. A. Sophian and F. H. Scharles, Kansas City.—p. 391.
Treatment of Acidosis in Renal Insufficiency. R. Deakin, St. Louis.—p. 394.
Undulant Fever. H. G. Newman, St. Louis.—p. 398.
Practical Methods of Case Finding. R. H. Runde, Mount Vernon.—p. 403.
Superior Pulmonary Sulcus Tumor Syndrome: Case Report. J. J. Gitt and E. H. Trowbridge Jr., St. Louis.—p. 405.

New England Journal of Medicine, Boston

219: 411-456 (Sept. 22) 1938

- Human Encephalitis Caused by Virus of the Eastern Variety of Equine Encephalomyelitis. L. D. Fothergill, J. H. Dingle, S. Farber and M. L. Connerley, Boston.—p. 411.
The Role of Rest and Exercise in Congestive Heart Failure: A Program for Treatment. D. Davis, Boston.—p. 412.
Two Years of Diabetic Surgery. B. Rabinovitz and J. Weisman, Springfield, Mass.—p. 423.
Ragweed-Pollen Survey in Maine for 1937. C. B. Sylvester, Portland, Maine, and O. C. Durham, North Chicago, Ill.—p. 428.
Diverticulum and Sarcoma of Duodenum: Report of Case. A. J. Mendillo and W. B. Koufinan, New Haven, Conn.—p. 432.
Progress in Dermatology. J. L. Grund, Boston.—p. 434.

219: 457-502 (Sept. 29) 1938

- Trauma Incident to Sports and Recreation. A. Thorndike Jr., Boston.—p. 457.
*Quantitative Differences in Effects of Alcoholic Beverages. H. W. Haggard, L. A. Greenberg and L. H. Cohen, New Haven, Conn.—p. 466.
Study of Seventy-Five Transfusions with Placental Blood. B. C. Grodberg and E. L. Carey, Boston.—p. 471.
The Relief of Chronic Backache and Sciatica by Minor Surgical Measures. W. A. Steel, Philadelphia.—p. 474.
Pneumococcal Pneumonia. F. T. Lord, Boston.—p. 483.

Effects of Alcoholic Beverages.—Haggard and his colleagues summarize the usefulness of blood tests for intoxication as follows: (1) demonstration that the blood contains no alcohol is absolute proof of nonintoxication, (2) the finding of alcohol in the blood demonstrates that alcohol has been consumed and (3) more than 1.5 mg. of alcohol per cubic centimeter of blood indicates definite intoxication. They performed numerous experiments on five young men ranging in weight from 150 to 175 pounds (68 to 79.5 Kg.). They were all moderate, occasional users of alcohol. On an empty stomach 63 cc. of 87 proof gin (containing 27.5 cc. of pure alcohol) induced a maximal blood concentration of alcohol of 0.54 mg. per cubic centimeter, while 126 cc. of gin induced a concentration of 1.01 mg. For 90 proof whisky the values for 61 cc. (27.5 cc. of pure alcohol) and 122 cc. were 0.51 and 0.89 mg. respectively. With an increase in the amount of spirit taken the alcohol in the blood does not rise proportionately. The relation is closer for gin than for whisky. Dilution lessens to some extent the concentrations of alcohol reached in the blood. A maximal concentration in the blood of 1.01 mg. was obtained when 126 cc. of straight gin was ingested on an empty stomach, while the same amount diluted to 1,000 cc. with water gave a maximum of 0.92 mg. Under the same circumstances the same amounts of alcohol as whisky gave maximal

values of 0.89 and 0.72 mg. respectively. While gin is absorbed more rapidly, it is also eliminated more rapidly. After drinking 55 cc. of alcohol as gin, the alcohol in the blood rose to 1.01 mg. per cubic centimeter but fell to 0.5 mg. in 105 minutes; after drinking the same amount of alcohol as whisky, the alcohol in the blood rose to only 0.89 mg. but did not fall to 0.5 mg. until 135 minutes later. Food in the stomach (within one hour after a breakfast of average size) greatly influenced the rate of absorption and consequently the maximal concentration of alcohol reached in the blood. The maximal concentrations induced by 126 cc. of 87 proof whisky were 0.89 mg. before a meal and 0.35 mg. after one; for the same amount of alcohol as gin the corresponding values were 1.01 and 0.41 mg. A few experiments with meals high in butter, olive oil and milk gave somewhat lower figures than for an average meal, but the results were not strikingly different. Alcohol, when taken as beer, is absorbed much more slowly than when taken as spirit—or even as diluted spirit—and the maximal concentration reached after a given amount of alcohol is lower. Thus while 55 cc. of alcohol as gin gave a maximal blood-alcohol concentration of 1.01 mg. and as whisky 0.89 mg., the same amount as beer (1,222 cc. of 4.5 per cent alcohol by volume) gave a concentration of only 0.44 mg. After a meal the maximum reached for the same amount of beer was 0.24 mg. The rate of absorption varies for the three beverages studied with the amount of buffer substances they contain. A trace of acid is sufficient to render gin acid; whisky requires somewhat more; for beer a considerable amount must be used. These differences suggest that the rate of absorption is influenced by the rate at which the beverage is passed into the intestine. The maximal concentrations in the blood would presumably be correspondingly increased or decreased for persons weighing much more or less than the authors' subjects.

Philippine Islands Med. Association Journal, Manila

18: 481-548 (Aug.) 1938

- Studies on Vitamin C: II. Determination of Vitamin C (Ascorbic Acid) in Philippine Vegetables by the Dye Method I. Concepcion, with technical assistance of Maria Luisa Gargaritano, Manila.—p. 481.
Respiratory Data Among Filipinos. N. Cordero, Manila.—p. 491.
Conservative Treatment of Eclampsia. Honoria Acosta-Sison and J. Villanueva, Manila.—p. 497.
Social Justice—and Our Injured Laborers. J. Santillan, Manila.—p. 501.
Preliminary Report on Ileocolostomy. J. Eduque and A. Tangco, Manila.—p. 507.

Public Health Reports, Washington, D. C.

53: 1635-1684 (Sept. 16) 1938

- *Incidence of Rheumatic Heart Disease Among College Students in the United States: Based on Replies to a Questionnaire. O. F. Hedley.—p. 1635.
Susceptibility of Mice to Spontaneous, Induced and Transplantable Tumors: Comparative Study of Eight Strains. H. B. Andervont.—p. 1647.
Incidence of Induced Subcutaneous and Pulmonary Tumors and Spontaneous Mammary Tumors in Hybrid Mice. H. B. Andervont.—p. 1665.

53: 1685-1732 (Sept. 23) 1938

- Studies on Dental Caries: VII. Sex Differences in Dental Caries Experience of Elementary School Children. H. Klein and C. E. Palmer.—p. 1685.
Studies of Sewage Purification: VII. Biochemical Oxidation by Activated Sludge. C. C. Ruchhoft, P. D. McNamee and C. T. Butterfield.—p. 1690.

Rheumatic Cardiac Disease in College Students.—Based on 104,163 student health examinations (from eighty-six colleges and universities) Hedley reports an incidence of rheumatic cardiac disease among men students of 9.5 per thousand, while that among women students was 14.9. In fifty-nine coeducational institutions the rate among 53,068 physical examinations on men students was 9 per thousand, while among 27,311 female students it was 11.9. In twenty-nine of these institutions the rate reported was higher among men students and in twenty-eight it was higher among women students, while in two the rates were practically the same. The incidence among 32,863 male students in the fourteen large universities with affiliated medical schools was 6 per thousand, while among 13,235 women students it was 7.4. In one large university, probably owing to some local condition, the rate among women students was

nearly 21. When this university is excluded, the rate among men students is 6.3 per thousand while that among women students is 6. It is extremely doubtful whether sex plays an important part in the incidence of rheumatic heart disease among college students.

South Carolina Medical Assn. Journal, Greenville

3-4: 201-226 (Aug.) 1938

Prostatoseminal Vesiculitis. H. Y. Harper, Anderson.—p. 201.
Blood Transfusion: Review of 1,000 Cases. G. R. Dawson, Charleston.—p. 207.

3-4: 227-250 (Sept.) 1938

Management of Complicated Labor in the Home. R. Torpin, Augusta, Ga.—p. 227.
Use of Hydrogen Peroxide as Diagnostic and Prognostic Test in Vaginitis. G. McCutchen, Columbia.—p. 230.
Growth of Tubercle Bacillus: Restraining or Inhibiting Effect of Carbon Dioxide: Case Report. W. T. Lander, Williamston.—p. 236.

Surgery, St. Louis

4: 321-482 (Sept.) 1938

Technic of Nailing of Fractures of Neck of Femur. C. Semb, Oslo, Norway.—p. 321.
Relief of Paroxysmal Hypertension by Excision of Pheochromocytoma. A. Brunschwig, Eleanor Humphreys and N. Roome, Chicago.—p. 361.
Malignant Perineal Tumor Simulating Inflammatory Lesions: Two Cases. R. M. Hosler and J. A. Murphy, Cleveland.—p. 371.
Congenital Anorexia: Report of Six Probable Cases of Monorchia. C. E. Rea, Minneapolis.—p. 376.
Torsion of Uterine Adnexa. E. A. Ficklen, New Orleans.—p. 384.
Cause of Death in Bile Peritonitis. M. H. Manson, New York, and C. T. Eginton, Minneapolis.—p. 392.
Subphrenic Abscess: Medical Review. W. A. Doidge and W. P. Warner, Toronto.—p. 405.
Palmar Fascia in Connection with Dupuytren's Contracture. E. B. Kaplan, New York.—p. 415.
Mixed Tumor of Parotid Gland with Metastasis: Case Report. W. P. Montanus, Cincinnati.—p. 423.
Lipiodol in Treatment of Persistent Fecal Fistula After Appendectomy. S. N. Mendelsohn and L. H. Schriver, Cincinnati.—p. 430.
Unusual Complication Following Suboccipital Craniectomy. M. W. Thorner and R. A. Groff, Philadelphia.—p. 434.

Cause of Death in Bile Peritonitis.—In order to demonstrate the noxiousness of intraperitoneal sterile bile and to determine the cause of death in choleperitoneum, Manson and Eginton subjected dogs and guinea pigs to procedures designed to imitate as closely as possible the circumstances under which the condition occurs clinically. From their experiments they conclude that there are at least two factors causing death in choleperitoneum: the primary injury to the peritoneum by the toxic bile salts and the secondary shock from the loss of fluid from the vascular system. The toxic effect of absorbed bile and the bacterial factor may be of importance but, if so, they are probably only contributory to the fatal outcome.

Tennessee State Medical Assn. Journal, Nashville

31: 337-380 (Sept.) 1938

Perforation of Intestines. E. D. Mitchell Jr., Memphis.—p. 337.
Maneuvers in Abnormal Second Stage of Labor. W. G. Rhea, Paris.—p. 344.
Treatment of Lobar Pneumonia. H. B. Gotten and R. E. Ching, Memphis.—p. 349.
Black Widow Spider Bites. H. T. Kirby-Smith, Winchester.—p. 357.
Treatment of Empyema: Tidal Irrigation. G. H. Kistler, Chattanooga.—p. 362.

Texas State Journal of Medicine, Fort Worth

3-4: 257-322 (Aug.) 1938

Cause and Treatment of Functional Uterine Bleeding. E. Novak, Baltimore.—p. 263.
Discussion of Obstetric Anesthesia and Analgesia Based on 5,000 Cases. E. D. Embree, Houston.—p. 268.
Gas Gangrene. R. J. White, Fort Worth.—p. 271.
New Surgical Procedure in Acute Infectious Arthritis: Preliminary Report. H. E. Hipps, Marlin.—p. 276.
End Result in 1,000 Consecutive Industrial Fractures. H. Poyner, Houston.—p. 284.
Radiation Therapy of Fungous Infections. D. Spangler, Dallas.—p. 289.
Study of the Incidence of Intestinal Parasites in 2,800 Persons in Dallas, Texas and Vicinity. H. E. Wright and W. H. Moursund Sr., Dallas.—p. 292.
Gastric Lesion Produced by Posterior Pituitary Extract. M. H. Metz, Dallas.—p. 295.
Management of Heterophoria. C. R. Hartsook, Wichita Falls.—p. 298.
Modern Immunization Program for Children. J. P. Gibson, Abilene.—p. 301.
Study of Morphine, Scopolamine and Atropine and Their Relation to Pre-operative Medication and Pain Relief. R. M. Waters, Madison, Wis.—p. 304.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

Archives of Disease in Childhood, London

13: 193-288 (Sept.) 1938

Wilms' Embryoma: Clinicopathologic Study. Ruby O. Stern and G. H. News.—p. 193.
*Esophagitis in Infancy. J. H. Ebbs.—p. 211.
Symmetric Degeneration of Neostriatum in Chinese Infants. W. J. C. Verbaart.—p. 225.
Clinical Ascariasis in Children. Cicely D. Williams.—p. 235.
Precocious Puberty: Report on Case of Pineal Syndrome. A. V. Neale.—p. 241.
Congenital Pyloric Stenosis in First and Second Cousins. E. A. Cockayne.—p. 249.
Nutritional Edema in Children in Egypt. H. Shukry, M. A. Mahdi and A. A. El Gholmy.—p. 254.
*Spontaneous Subarachnoid Hemorrhage in Children: Clinical Study of Five Cases. H. G. Miller.—p. 258.
Congenital Hemolytic Anemia with Normal Fragility of Red Blood Cells. E. Schiff.—p. 264.

Esophagitis in Infancy.—In a review of the records of the Birmingham Children's Hospital for the last three years, Ebbs found that, whereas thirty-one children have been admitted for treatment of foreign bodies in the esophagus, poisoning and congenital strictures, twenty-eight children have died with an acute esophagitis. The age of the former group was between 1 and 12 years and those with acute esophagitis were less than 10 months of age, the average being 4 months. Thrush was the etiologic factor in twenty-two cases, diphtheria in two, tuberculosis and Vincent's organism in one each, and in three there was ulceration and inflammation of the esophagus without a specific organism being demonstrated.

Spontaneous Subarachnoid Hemorrhage in Children.—Five cases of spontaneous subarachnoid hemorrhage are reported. Although neither of the two fatal cases came to necropsy, Miller states that the diagnosis in every instance was confirmed by examination of the cerebrospinal fluid. The clinical picture in all five cases was so strikingly similar to that known to occur in adults that in the three cases in which there were no complicating factors similar pathologic changes are suspected. Intracranial aneurysm of the type that gives rise to subarachnoid hemorrhage in the healthy young adult has not been recorded frequently in children, but if, as structural evidence suggests, these aneurysms are truly congenital in nature, they must obviously be present (perhaps on occasion only) at birth. The frequently reported association between intracranial aneurysm and coarctation of the aorta is further evidence in favor of a congenital origin, and Fearnside reports one significant case of a definite aneurysm of the circle of Willis found at necropsy in a child of 19 months dying of bronchopneumonia complicating gastritis. It is suggested that in three of the cases the hemorrhage was in all probability due to rupture of a congenital intracranial aneurysm and that pathologically as well as clinically these cases are analogous to spontaneous subarachnoid hemorrhage occurring in adults. One of the other two patients was at stool when the hemorrhage with loss of consciousness occurred, while the other patient had a facial hemangioma, and some similar intracranial pathologic change is suspected as the cause of the hemorrhage. The pyrexial phenomena associated with the hemorrhage were somewhat inconstant as compared with those occurring in adults.

British Medical Journal, London

2: 555-604 (Sept. 10) 1938

Occipitoposterior Positions of Vertex and Their Complications. C. Moir.—p. 555.
*Interruption of Early Pregnancy by Means of Orally Active Estrogens. A. S. Parkes, E. C. Dodds and R. L. Noble.—p. 557.
Observations on Treatment of Empyema in Children. H. L. Wallace.—p. 560.
Synergy in Experimental Chemotherapy of Staphylococcal Infections. S. P. De and U. P. Basu.—p. 564.
Daylight in Relation to Climate and Health. W. R. G. Atkins.—p. 565.

Interruption of Early Pregnancy by Estrogens.—Parkes and his colleagues investigated the capacity of two estrogenic substances (from 0.25 to 1 mg. of ethinyl estradiol and from 1 to 4 mg. of diethylstilbestrol), given orally, to suppress the action of progesterone and to prevent pregnancy. The

substances were fed to rabbits in propylene glycol solution, which was swallowed readily. They found that small doses of orally active estrogen will prevent implantation of the blastocyst if given soon (two to seven days) after ovulation or may terminate established pregnancy. The effect is produced in what is essentially a physiologic manner: the luteal phase of the cycle is suppressed and another phase is induced which, though not abnormal in itself, is unsuitable for the development of the embryo. Everything that is known about the menstrual cycle of primates suggests that its hormone control is the same as in lower animals and it is extremely probable that the factors governing the implantation of the fertilized egg are fundamentally similar in women. The conclusions arrived at should thus be applicable to women, though the fact that very large amounts of estrogen are excreted by pregnant women makes it likely that the period during which estrogenic treatment might be effective would be relatively much shorter than in rabbits.

2: 605-644 (Sept. 17) 1938

Vertigo: Its Neurologic, Otologic, Circulatory and Surgical Aspects. W. R. Brain.—p. 605.

Cooperation Between Ophthalmologist and Physician in Certain Cases of Visual Loss. C. B. F. Tivy.—p. 608.

*New Type of "Jacket" Respirator for Treatment of Poliomyelitis. A. F. Burstall.—p. 611.

Diagnosis of Whooping Cough. A. B. Donald.—p. 613.

Human Oil in Treatment of Adherent Scars. C. P. G. Wakeley.—p. 618.

New Respirator for Poliomyelitis.—Burstall describes a jacket respirator that consists of an aluminum cuirass made in one piece, which is hammered out to the shape of the thorax. It encloses the trunk of the patient from the neck down to the waistline and is connected to the pulsating apparatus by a 1 inch flexible hose. It can be connected to a respirator of cabinet type. The capacity of a cuirass is so small that a large number of them may be operated from one cabinet type respirator by drilling a hole in the cabinet and connecting a hose to it. Inside the cuirass is a sponge rubber vest, 1 inch thick, with holes for the arms, neck and waist. The openings in the cuirass have a beaded edge and are closed to the body by soft sheet rubber jointing pieces, which are held to the cuirass by being lifted over the beaded edge. Rubber rings may also be added to prevent the sheet from working off the beaded edge. The cuirass is provided with four metal lugs for the attachment of arm splints. The whole of the metal work can be sterilized. It weighs only 6 pounds for a patient 10 years of age. Three sizes of cuirass will provide for patients ranging from the age of 3 years up to medium-sized adults. The time taken for two persons to dress a sick patient completely in the new respirator is seven minutes without splints and from ten to twelve minutes with splints. This respirator is therefore not as suitable for the treatment of emergency cases as respirators of the Drinker type.

Edinburgh Medical Journal

45: 605-664 (Sept.) 1938

Experimental Neuroses in Animals and Their Treatment with Bromides. B. P. Babkin.—p. 605.

Right-Sided Aortic Arch. J. P. McGibbon.—p. 620.

William Osler. J. Hay.—p. 631.

Pernicious Anemia and Its Treatment. A. Goodall.—p. 648.

Biologic Properties of Killed Tubercle Bacilli Deprived of Acid-Fastness by Method of Browning and Gulbransen. Mary A. Griffin.—p. 654.

Glasgow Medical Journal

12: 109-172 (Sept.) 1938

Nonsurgical Treatment of Cataract. J. Burdon-Cooper.—p. 109.

Guy's Hospital Reports, London

88: 257-370 (July) 1938

Arthur Edwin Boycott. G. W. Goodhart.—p. 257.

Studies on Tumor Formation. G. W. Nicholson.—p. 263.

Granulosa Cell Ovarian Tumor as Cause of Sexual Precocity: Report of Case. Min Sein.—p. 299.

Head Noises and Cranial Bruits. W. G. Sears.—p. 308.

Report on Cases of Perineal Swellings Due to Inflammation and Other Causes Occurring in Genito-Urinary Department at Guy's Hospital, 1910 to 1936. A. R. Thompson.—p. 320.

Psychologic Investigation of Case of Dermatitis Artefacta. F. W. Brown.—p. 356.

Importance of Breast Feeding in Prevention of Diarrhea and Vomiting of Infancy. N. M. Jacoby.—p. 367.

Irish Journal of Medical Science, Dublin

No. 152: 341-596 (Aug.) 1938

Report of the Rotunda Hospital (Nov. 1, 1936, to Oct. 31, 1937).

A. H. Davidson, R. C. Sutton and J. B. Fleming, G. Dockery, C. L. McDonogh and W. R. F. Collis.—p. 341.

Clinical Report of the Coombe Lying-in Hospital, 1937. R. M. Corbet, J. A. Finegan and J. K. Feeney.—p. 438.

Clinical Report of the National Maternity Hospital. J. F. Cunningham, P. J. McMahon and J. Gallagher.—p. 511.

Note on Speculum Matricis of James Wolveridge. T. P. C. Kirkpatrick.—p. 577.

A Visit to the Clinics of Frankfurt and Heidelberg. R. M. Corbet.—p. 578.

Journal of Tropical Medicine and Hygiene, London

41: 261-276 (Aug. 15) 1938

Protective Inoculation Against Typhus. M. A. Gohar.—p. 261.

Fourth Note on Infectivity to Man of Strain of Trypanosoma Rhodesiense. J. F. Corson.—p. 262.

Trypanosomiasis Gambiense: Some Observations in Uganda and Their Bearing on Prophylaxis. A. A. F. Brown.—p. 265.

Lancet, London

2: 651-704 (Sept. 17) 1938

*Severe Hemorrhage from Stomach and Duodenum. T. I. Bennett, J. Dow, F. P. L. Lander and S. Wright.—p. 651.

Some Observations on Arches of Foot and Flat Foot. J. Bruce and R. Walmsley.—p. 656.

Corarctation of Aorta: Report of Two Cases. Joan B. Walker and F. D. M. Livingstone.—p. 660.

Fits and Schizophrenia. S. W. Gillman and D. N. Parfitt.—p. 663.

Ketoneuria in Diabetes and Pregnancy. C. H. Gray.—p. 665.

Staphylococcal Septicemia Treated with 2-(p-aminobenzenesulfonamido) Pyridine. W. J. Fenton and F. Hodgkiss.—p. 667.

Facial Carbuncle Treated with Protosil Album: Personal Experience, with Note on Its Effect in Lupus Erythematosus. H. W. Barber.—p. 668.

Immunologic Connection Between Burns and Sepsis. W. H. Hughes.—p. 670.

Hemorrhage from Stomach and Duodenum.—Bennett and his colleagues studied 122 cases in which life was endangered by gastric and duodenal hemorrhage. The severity of any case can be judged only when it is known how much blood has been lost and whether bleeding has ceased, temporarily or permanently. Determinations of the volume of blood lost revealed that in thirty-three cases the amount of blood lost did not amount to more than one fifth of the total blood volume, while in thirty-two it was not more than one half. That the estimation of blood volume is a genuine criterion of severity is indicated by the fact that the fatal cases were confined to the group in which the volume of blood was notably reduced (more than 50 per cent). It is to be noted that it is the fraction of the total blood volume consisting of the cells which is the all important one. The total blood volume is also the only certain guide available for the determination of whether actual hemorrhage has ceased or not. In the hours after hemorrhage has begun the hemoglobin percentage must be expected to continue to fall for some time whether the actual hemorrhage has ceased or not. Though it is true that, if hemorrhage is continuing the fall of hemoglobin may be greater than if it has been arrested, this is not necessarily so owing to the variation in the intensity of the bleeding from case to case. The one fact which points inevitably to the conclusion that bleeding is still in progress is that the cell volume has diminished in the second case whereas it remains unchanged in the first.

Medical Journal of Australia, Sydney

2: 405-446 (Sept. 10) 1938

Diverticulosis and Diverticulitis. C. B. Blackburn.—p. 405.

Diverticulosis and Diverticulitis from Radiologic Point of View. H. R. Sear.—p. 409.

Occurrence of Juxta-Articular Nodules in Australia. F. J. Fenner.—p. 412.

Some Aspects of Psittacosis and Isolation of Virus. A. R. Tremaine.—p. 417.

Some Observations on Use of Protamine Zinc Insulin in Management of Diabetes Mellitus. E. Downie.—p. 421.

South African Medical Journal, Cape Town

12: 569-612 (Aug. 27) 1938

Pancreatitis. A. Radford.—p. 585.

Pellagra. L. R. Brumberg.—p. 587.

Malarial Pyrotherapy for Syphilitic Disease of the Central Nervous System. D. S. Huskisson.—p. 589.

Insulin Therapy. J. A. Higgs.—p. 590.

Colospasm. R. Schaffer.—p. 594.

Archives des Maladies du Cœur, Paris

31: 765-884 (Aug.) 1938. Partial Index

- Experimental Contribution to Physiopathology of Arteriovenous Aneurysm. A. Tournade and E. Curtillet.—p. 766.
- Paroxysmal Ventricular Tachycardia in Experimental Auriculoventricular Block. R. Froment and F. Jourdan.—p. 792.
- Electrocardiographic Studies in Course of Treatment of Schizophrenia with Metrazol. E. Gérardel.—p. 811.
- Cardiac Automatism. E. Donzelot.—p. 817.
- *Therapeutic Action of Adenosine. R. Fabre.—p. 824.
- Rheumatismal Auriculoventricular Block. C. G. Marchal, J. Lenègre, Bussion and Mathivat.—p. 844.

Therapeutic Action of Adenosine.—Fabre says that animal experiments with adenosine revealed that this substance has a notable vasodilating effect on the coronary vessels. He regards the hyposensitive effect observed by some as of slight importance, because in his own experiments on dogs he found that the decrease in arterial pressure is of only short duration (a few seconds). Moreover, adenosine seems to have no toxic effect if it is given in suitable doses. On the basis of experimental results and encouraged by the therapeutic effects obtained in human subjects by the oral administration of adenosine, the author decided to try the intramuscular injection in daily doses of from 5 to 10 mg. (2.5 mg. per cubic centimeter of physiologic solution of sodium chloride). He reviews the clinical histories of ten patients with symptoms of angina pectoris in whom he resorted to the intramuscular injection of adenosine. Some of the case histories indicate that he administered 5 mg. at each injection and that the total number of injections varied between six and twelve. In eight of the ten patients the intramuscular injections of adenosine proved effective but in two cases they had no effects on the anginal symptoms. This failure in some cases the author regards as additional proof of the fact that the pathogenic mechanism of the anginal syndrome is not the same in all cases.

Presse Médicale, Paris

46: 1385-1400 (Sept. 17) 1938

- General Review of Influenza: Anti-Influenzal Serum Therapy. A. Bédère.—p. 1385.
- *New Method of Treatment for Dermal Leishmaniasis (Oriental Sore). F. Flarer.—p. 1388.

New Treatment for Dermal Leishmaniasis.—Dermal leishmaniasis being comparatively frequent in Sicily, and its treatment not being entirely satisfactory as yet, Flarer decided to try the antiprotozoal medicament atabrine, which had been found highly effective not only in the treatment of malaria but also in another protozoal disease, namely lambliasis. The author describes his experiences with this treatment in fourteen cases of dermal leishmaniasis. In the first four cases he combined general and local treatment. The general treatment consisted either in the oral or in the intravenous administration of the medicament. Although it improved the local lesions and reduced the number of protozoans, they did not completely disappear until local treatment was instituted. In the first case, the author says, it was given in the form of intradermal injections so as to soak the entire ulceration with atabrine dissolved in distilled water. The slight edema which followed persisted for about twenty-four hours, but without a trace of inflammatory reaction and without noticeable local pain. The ulceration regressed rapidly and the protozoans disappeared and remained absent after a month of observation, in the course of which the ulceration had been smoothed out. This and three other cases, in which general and local treatment was used, having convinced the author that the local treatment was the more effective, he used local treatment exclusively in the other ten cases of dermal leishmaniasis. In four cases he tried half doses (0.05 Gm. of atabrine) repeated twice at three day intervals. Since the local tolerance was excellent, he later administered 0.1 Gm. of atabrine dissolved in 1 or 2 cc. of distilled water, depending on the size of the ulceration. This treatment was followed by permanent cure with disappearance of the protozoans, even after a single injection. The author concludes that it is unquestionable that this treatment has advantages over all of those hitherto employed.

46: 1401-1416 (Sept. 21) 1938

- Vascular Therapy in Aortic Insufficiency and in Mitral Insufficiency. A. Ferrannini.—p. 1401.
- Gangrene of Extremities of Venous Origin. M. Audier and H. Haimovici.—p. 1403.
- *Role of Vitamin B₁ in Humoral Regulation of Nervous System: Therapeutic Suggestions. B. Minz.—p. 1406.

Vitamin B₁ and Nervous System.—Minz reviews Loewi's theory of the humoral transmission of the nervous impulse which assumes the liberation of two antagonistic substances at the nervous terminations, one of the type of acetylcholine and another of the type of epinephrine. After citing recent investigations on the role of acetylcholine in the excitation of the nerves, he reports some of his own observations which suggested to him that the extract of the nerve that had been subjected to excitation contained, in addition to the substance of the acetylcholine type, a second substance which reinforced the action of the first. Investigations on the nature of this substance disclosed that its action was like that of a ferment. Consequently he searched for a substance with this type of action in yeast, and experience confirmed the supposition that this substance exists in yeast. In view of the fact that yeast is rich in vitamins, particularly the vitamins the deficiency of which produces nervous disturbances, he investigated whether the substance might perhaps be identical with the antineuritic factor, that is, vitamin B₁. He was able to show that vitamin B₁ is capable of strengthening the effect of acetylcholine and that in the humoral mechanism of nervous excitation vitamin B₁ assumes a role of coferment of acetylcholine. He shows that the strengthening of the actions of one of these agents by the other is not only of scientific but also of practical interest. On the one hand it may serve as a basis for the interpretation of the syndrome of B₁ avitaminosis and of related conditions; on the other hand it is of value for the therapy of a group of nervous disturbances. The absence of the coferment of the acetylcholinic action explains some symptoms of beriberi such as tachycardia, the disappearance of the patellar and achilles tendon reflexes, the disturbances of coordination, the atrophy of the muscles and the neuritic, paralytic and gastrointestinal disorders. Moreover, it is known that several of these phenomena are present in febrile diseases such as malaria, typhoid, dysentery and pneumonia and even in the banal infections. Finally they are observed in the course of conditions which are accompanied by an augmentation of the metabolism (pregnancy, lactation and physical exertion). It appears that these symptoms are brought on by the factors which increase the organism's need for vitamin B₁. Among the agents which disrupt the optimal equilibrium between acetylcholine and vitamin B₁ there is, in addition to certain micro-organisms, also the cancerous cell, a fact which is of great importance for the study of cancer. Favorable therapeutic effects of vitamin B₁ have been observed in cases of neuritis and even in several cases of multiple sclerosis, also in the nervous symptoms of pernicious anemia. Discussing the latter disease, the author points out that favorable therapeutic results have been obtained with acetylcholine. However, because the action of this substance is of extremely short duration, he thinks that the preliminary administration of vitamin B₁ will make the action of acetylcholine more intensive and lasting.

Schweizerische medizinische Wochenschrift, Basel

68: 1089-1108 (Sept. 24) 1938. Partial Index

- Present Status of Research on Hormones in Gynecology. O. Koller.—p. 1089.
- *Epidemic Myalgia (Bornholm Disease). E. Jenny.—p. 1092.
- Pathogenesis of Pulmonary Collapse by Blockage of Air Passages. Hilde Lachmann-Mosse.—p. 1094.
- Investigations on Antigenic Function of Vitamin A. J. P. Klapczak.—p. 1098.

Epidemic Myalgia.—Jenny reports the clinical histories of two brothers aged 9 and 8 years. The 9 year old boy became ill with sudden fever and headache. Then he developed severe muscular pains especially in the lower part of the thorax and over the stomach. The pains became exacerbated in successive attacks and were felt especially during deep respiration. The epigastric region was highly sensitive to the touch and the right abdominal rectus seemed slightly swollen. Coughing and other catarrhal symptoms were lacking. There were no pneumonic murmurs or pleuritic rub. Following a temporary sub-

sidence of the pains and fever they recurred once more, but then they subsided again and after six days the boy was well again. Two days after this boy had become ill his younger brother showed the same symptoms. The author had never encountered this disorder but recalled having read about the occurrence of epidemic myalgia in the Scandinavian countries. Reviewing the literature on this disease, he points out that it appears in smaller or larger epidemics, especially during the summer and fall months. It attacks chiefly young persons and children. The incubation period varies between two and four days. Infectiousness has been known to persist for four weeks after the recovery of the patient. The myalgia involves chiefly the intercostal muscles, the diaphragm and the abdominal recti and obliqui. This explains why respiration, particularly the inspiration, is so painful and why the respiration is superficial and accelerated, so that pneumonia or pleurisy may be thought of. The severe muscular pains have been compared with "stitches in the side" and in the popular language they have led to such designations as "lung stitches" or "devil's grip." The involved musculature is sensitive to pressure, but the skin is not hypersensitive. Swelling or hardening of the muscle is observed in some instances. The disease usually persists for eight or ten days. The prognosis is favorable for the myalgia as well as for the complications. The therapy is purely symptomatic. The etiology and pathogenesis are still unknown, but many observers assume that it is a virus disease. Reviewing the geographic distribution of epidemic myalgia, the author points out that since Sylvest's description of an extensive epidemic on the Danish island of Bornholm the disease has been known also under the term of Bornholm's disease. Regarding the probable origin of the cases here described, he says that the father of the boys had attended a course in which sixty-two Danes participated, and inquiry in Denmark disclosed that cases of epidemic myalgia had occurred there during July and August. It is possible that one of the men from Denmark was a virus carrier.

Annali dell'Istituto "Carlo Forlanini," Rome

2: 437-576 (July-Aug.) 1938. Partial Index

- *Influence of Pneumoperitoneum on Electrocardiogram. V. Agnello.—p. 437.
- Partial Pneumothorax and Elastic Anterolateral Thoracoplasty. S. Gunella.—p. 445.
- Electrocardiographic Researches in Deviation of Mediastinum in Course of Artificial Pneumothorax. V. Agnello.—p. 461.
- Pneumoperitoneum in Abdominal Disturbances from Pleurisy. P. Guglielmetti.—p. 489.

Influence of Pneumoperitoneum on Electrocardiogram.

—Agnello observed the behavior of the electrocardiogram before and after establishment of pneumoperitoneum in twenty patients suffering from tuberculosis. Collapse treatment, especially by artificial pneumothorax, was already established in the majority of the cases. The electrocardiograms were taken of patients at rest and during fasting, immediately before and after an insufflation of about 300 cc. of oxygen into the peritoneal cavity. Pneumoperitoneum induced an increase of the pause between two consecutive cardiac revolutions (atrioventricular complexes), as shown by the prolongation of the TP space in the electrocardiogram and also alterations of the R, S and T waves in the three leads. According to the author the electrocardiographic alterations are due to deviations of the electrical axis from displacement of the heart and also to functional changes of the heart from vagosympathetic stimulation. The functions of the heart are good in pulmonary tuberculosis before and after establishment of collapse of the lung and of pneumoperitoneum. The latter has both a mechanical action and a capacity of stimulating the sympathetic nervous system.

Minerva Medica, Turin

2: 197-220 (Sept. 1) 1938

- Undulant Fever with Hemorrhagic Purpura of Werlhof's Type and Hypoplastic Global Myelosis. O. Da-Rin.—p. 197.
- *Hydronephrosis and Abnormal Renal Vessel: Clinical Study. L. Annibaldi.—p. 205.

Hydronephrosis and Abnormal Renal Vessel.—Annibaldi

reports seven cases of hydronephrosis in persons having a vessel of abnormal course. According to the author the ptosis of the kidney, the various congenital malformations existing in cases of abnormal renal vessels and the presence of general or local

infection are the main causal factors of hydronephrosis. The pathogenic role of the vessel is of secondary importance. A renal artery, especially a branch of the renal artery or of the aorta, follows an abnormal course more frequently than a renal vein. Generally the vessel follows an oblique downward direction to the lower pole of the kidney and it embraces the ureter either anteriorly or posteriorly. The diagnosis of the condition is made by roentgen examination of the kidney and of the urinary tract and ascending pyelography when hydronephrosis is already established and by pyeloscopy early in the development of pelvic stagnation which precedes hydronephrosis. The treatment is surgical. If the function of the involved kidney is good, conservative treatment is advisable. Otherwise nephrectomy is indicated, especially if the parenchyma of the involved kidney shows grave changes or if there is a renal infection.

Rivista di Neurologia, Naples

11: 281-376 (Aug.) 1938

- *Neurologic Syndromes of Recklinghausen's Neurofibromatosis. F. Vizioli and S. Tolone.—p. 281.
- Cerebral Multiple Tumor (Glyoblastoma) of Pons and Corpus Callosum Without Psychic Syndromes. D. Alessi.—p. 321.
- Spasmodic Scoliosis in Differential Diagnosis Between Symptomatic Lumbar Ischialgia from Compression of Cauda Equina and Idiopathic Lumbar Ischialgia of Long Duration. C. Masci.—p. 340.

Neurofibromatosis.—Vizioli and Tolone report four cases

of diffuse neurofibromatosis of Recklinghausen's type, with important peripheral and central neurologic complications. In the first case the neurologic symptoms were those of an intramedullary tumor at the cervical segment of the spinal cord with formation of intratumoral cavities of the syringomyelic type. The second patient showed cerebral symptoms from bilateral multiple neurofibroma of the posterior cranial fossa (deafness, blindness and disturbances in walking). He had a nodule at the right laterocervical region which for the last few months had been painful on pressure and followed a rapid development. The nodule was removed. It was found that it had been transformed into sarcoma of the neurofibromatous type which does not produce metastases. The third patient had suffered in childhood from a nervous disease (either poliomyelitis or poliomyelitis) from which residual left facial paralysis and atrophic paralysis of a leg remained. He showed symptoms of compression of the cervical segment of the spinal cord from an extramedullary tumor which seemed to originate in the distal roots of the right cervical nerves. The fourth patient had a complete spastic paraplegia with contracture in flexion from spinal trauma. The neurologic syndrome consisted in complete flaccid paralysis of the left arm from compression of the brachial plexus by a large fibrosarcoma deeply seated in the axillary cavity. The patient had in association an incomplete acromegalic syndrome. The author made a microscopic study of the tumors removed by operation, of the cutaneous nodules and of some neurofibromas, taken by biopsy in all but the first case, which was the most simple. He found that the skin nodules and an extramedullary tumor had the typical microscopic aspect of neurofibromatosis of Recklinghausen's type. The tumor showed sarcomatous degeneration in two cases. Some oligodendroglioma of the first (Robertson) and second types (Cajal) were identified in the preparations of neurofibroma. In connection with the cases reported the author discusses the pathogenesis of neurofibromatosis of Recklinghausen's type, which he believes originates in defective development of the nervous system during embryonal evolution. The endocrine disorders that precede or are associated with the disease are secondary factors.

Deutsche Zeitschrift für Chirurgie, Berlin

250: 705-756 (Aug. 31) 1938

- Nerve Apparatus of Human Lung and Its Clinical Significance. P. Sunder-Plassmann.—p. 705.
- *Surgery of Funnel Shaped Chest. H. Krauss.—p. 715.
- Contributions to Hemorrhage at Base of Skull. O. Voss.—p. 727.
- Cystic Lymphangioma of Small Intestine. V. Pliverić.—p. 736.
- Tumor of Colon in a Hernial Sac. F. Gerhardt.—p. 742.

Surgery of Funnel Shaped Chest.—According to Krauss the congenital type of funnel shaped chest is characterized by the fact that it becomes deeper with the growth of the person

and the transverse diameter of the thorax larger. The deformity is as a rule symmetrical with the deepest point opposite the ninth and tenth thoracic vertebrae. The deformity affects the mediastinal organs and the respiratory movements. The clinical symptoms depend on the depth of the depression and the capacity of the intrathoracic organs to accommodate themselves to the altered mechanical relationship. The majority of the children so afflicted do not present functional disturbances of any kind. In a small proportion of the cases the deformity results in a narrowing of the chest and a marked dislocation of the mediastinal structures. The distance between the posterior wall of the sternum and the vertebral bodies may be shortened by several centimeters. The heart may become displaced to the left and the venae cavae compressed, leading to stasis, distention of the veins of the neck, cyanosis and dyspnea. The more or less fixed thoracic wall interferes with respiratory movements and leads to hypoventilation of pulmonary tissue. Such patients complain of shortness of breath, frequent attacks of bronchitis, palpitation, weakness and early fatigue; difficulty in swallowing and asthmatic attacks may occur. The aim of the operative intervention, according to the author, is the enlargement of the mediastinal space. The loss of the sternum, however, deprives the mediastinal structures of their protection as well as causes the direction in which the ribs move to be altered. In 1931 Sauerbruch and Nissen devised an operation in which the mediastinal space was enlarged by advancing the sternum in line with the thorax. It consisted of linear sectioning and removal of small portions of cartilages from the fourth to the eighth ribs on the left side at one sitting, while at the second sitting wire sutures were introduced through the right side of the sternum and attached to an extension apparatus. In the course of eight days the sternum was advanced so as to arrive at the level of the thorax. Ombrédanne's T shaped osteotomy, while effective, had a high immediate mortality, presumably caused by too sudden alteration in the position of the heart and the large vessels. The danger attendant on all types of operations is tearing of the pleura and subsequent pleural extravasation.

Münchener medizinische Wochenschrift, Munich

85: 1337-1376 (Sept. 2) 1938. Partial Index

- *Ocular Origin of Migraine in Children and Young Persons. K. Grunert.—p. 1337.
Recognition of Disposition for Cancer: Laboratory Tests for Detection of Disposition. J. Kretz.—p. 1341.
Quinine as Abortifacient. Koopmann.—p. 1344.
Irradiated Fresh Milk for Continuous Feeding. K. Scheer.—p. 1346.
Hypertrophy of Prostate: Diagnosis and Treatment. E. Thiermann.—p. 1347.

Ocular Origin of Migraine in Children.—For a period of ten years, Grunert made careful functional tests on the eyes of all patients who were subject to headaches and to migraine and, as far as possible, of the relatives of these patients who were subject to headaches. In the course of these studies he made two significant observations: 1. In the majority of the patients with headaches and in nearly all of those with migraine there existed disturbances in the ocular function. 2. The treatment of these ocular disturbances reduced or completely removed the general symptoms to such an extent that a causal connection could not be denied. In children and young persons the ocular origin of migraine was even more pronounced than it was in adults. The author reports observations in more than 200 cases of migraine in children and young persons. Many of the patients were of the type referred to as "difficult" children; that is, they showed signs of nervous irritability, they were difficult to manage or were inattentive in school and so on. Ocular examination disclosed defective refraction, disturbances in the ocular equilibrium and defects in the accommodation. In many of these children the growth of the eyes is not completed as early as in others and school, requiring a considerable amount of close work, involves a great strain on these still growing eyes. After describing some of the difficulties of these children and of the symptoms likely to develop in them, the author gives his attention to the treatment of the migraine of ocular origin. He emphasizes that even slight optic defects may cause severe subjective disturbances. After the refractive defects

have been corrected, close work is avoided for one or two weeks and the weakened muscle of accommodation is treated with pilocarpine. The administration of pilocarpine must be individualized. It is best to administer it in the evening before the patient goes to sleep. In severe cases it can be given also during the day, but in this case the individual doses are, of course, smaller. In case of disturbances in the muscular equilibrium or in latent strabismus, prisms are employed; occasionally an operation for strabismus may be resorted to or stereoscopic exercises may be employed. In the few cases in which no anomalies of refraction exist and in which there is no impairment of the muscular equilibrium, but only an insufficiency of the apparatus of accommodation, the migraine is cured by resting the eyes for a while and by treatment with pilocarpine. The ocular treatment effected cure in 197 children and young persons with migraine. The author closes his report by recommending that all children in whom migraine is suspected be subjected to a thorough examination of the eyes.

Zeitschrift für Kinderheilkunde, Berlin

60: 77-180 (Aug. 26) 1938. Partial Index

- *Development of Bacteria and of Lactic Acid in Milk to Which Citric Acid Has Been Added. W. Goeters.—p. 77.
*Fermentation of Citric Acid by Bacteria. W. Goeters.—p. 87.
*Changes Caused by Citric Acid Milk in Qualitative Composition of Bacterial Flora in Stools of Nurslings. W. Goeters.—p. 92.
Prognosis of Tuberculosis in Nurslings and Small Children. J. Bettle.—p. 95.
Westphal's Sign in Diseases of Cerebellum. Eleonore von Kirschtien.—p. 128.
Method for Counting Thrombocytes in Children. E. Lorenz.—p. 142.
Specific Serotherapy and Malignant Diphtheria. F. Tecilazic.—p. 172.

Bacteria and Lactic Acid in Milk Treated with Citric Acid.—After pointing out that the various dilutions of milk (half-milk, third-milk and so on) are not only superfluous but may even be harmful in the treatment of nurslings, Goeters says that it has been proved that whole milk which has been treated with lactic acid is superior to all types of diluted milk. He says that the favorable effects obtained with buttermilk in the treatment of dyspeptic nurslings are probably not so much the result of the acidity of this type of milk as of its comparatively high lactic acid content. However, not only lactic acid but other organic acids, particularly citric acid, have been found valuable as additions to whole milk in the feeding of nurslings. Some pediatricians regard citric acid as better for this purpose than lactic acid. After citing some previous studies on citric acid milk and experiences with it, the author describes bacteriologic studies which he himself made on whole milk to which citric acid had been added. He found that this type of milk promotes the growth of the most important lactic acid bacteria (lactic acid streptococci, beta cocci, *Bacterium lactis aerogenes*) but that it suppresses the development of *Bacterium coli*, micrococci and tetracocci and that it leaves other types of bacteria (*Bacillus proteus* and *Bacillus subtilis*) entirely unchanged. The percentage of lactic acid produced by bacterial action in citric acid milk is such that it exerts a favorable influence on the metabolism of healthy nurslings.

Fermentation of Citric Acid by Bacteria.—Goeters investigated whether citric acid serves as a source of carbon for the most important milk or fecal bacteria. He found that in citric acid milk as well as in synthetic nutrient solutions *Bacterium lactis aerogenes*, beta cocci, *Bacillus proteus* and *B. subtilis* and the majority of milk or fecal streptococci, with the exception of *Streptococcus cremoris* and *Streptococcus mastitidis*, act as fermenters of citric acid. The author regards it as especially important that, of twelve different strains of *Bacterium coli* which were tested, not a single one withdrew carbon from citric acid.

Changes Caused by Citric Acid Milk in Stools of Nurslings.—Goeters found that citric acid milk produces a change in the fecal flora of nurslings in that the lactic acid bacilli increase in number, whereas *Bacterium coli* and the putrefactive bacteria are reduced. The ratio of *Bacterium coli* to putrefactive bacteria to lactic acid bacteria (*Bacterium coli* taken as 1) changes from 1:1.3:1.2 to 1:0.5:5.1 mean value. At the same time, feces and urine have a strongly acid reaction.

The stools that are evacuated after feeding with citric acid milk resemble those of breast-fed infants. A few days after the feeding with citric acid milk is changed to feeding with a different formula, the lactic acid bacteria decrease greatly.

Nederlandsch Tijdschrift v. Geneeskunde, Amsterdam

82:4055-4150 (Aug. 20) 1938. Partial Index

*Further Observations on Hypophysis-Endocrine Reactions in Tuberculous Infections. L. Koster and R. de Boer.—p. 4062.

Occurrence of Postvaccinal Encephalitis in Young Children. H. W. Julius.—p. 4071.

Pulmonary Complications During Metrazol Treatment of Patients with Psychoses. A. J. van de Graaff, G. van Montfrans and G. Brouwer.—p. 4078.

Treatment of Addison's Disease. C. L. de Jongh.—p. 4082.

Hypophysis-Endocrine Reactions in Tuberculous Infections.—Koster and de Boer in 1935 described a syndrome which occurs in tuberculosis and which is characterized by obesity, erythremia, hypertension, purplish red striae, hyperglycemia, glycosuria, hyperthermia, moderate increase in the cholesterol content of the serum, increase in the basal metabolism and genital anomalies. Because these symptoms are the same as those that have been observed in hypophysial disorders, hypophysial anomalies have been regarded as a causal factor. In the course of the last several years the authors observed additional cases, and in this report they review fourteen in all. They investigated especially the cholesterol ester rate and the lipase content of the serum of these patients. They found that these values are increased in these patients, which is an indication of a hyperfunction of the hypophysis or at least of some of its elements. That this hypophysial disorder is especially frequent in tuberculosis the authors regard as a result of the fact that the immunity reactions of tuberculosis are entirely different from those of other infections. They consider the hypophysial hyperfunction as a form of defense reaction.

Hospitalstidende, Copenhagen

81:833-860 (Aug. 30) 1938

*Kraurosis of Vulva. K. E. Christensen.—p. 834.

Retromediastinal Goiter, Diagnosed by Aspiration Biopsy: Case. K. Roholm.—p. 853.

Kraurosis of Vulva.—The first, second and fourth of Christensen's four patients with kraurosis observed in 1937 were over 60 years of age and had had no symptoms of the lesion until fifteen or twenty years after the menopause; the third patient, aged 44, was still menstruating. Hormone analyses made in this case showed no insufficiency. All had had pruritus of the vulva, typical of the lesion, for from three months to seven years, with characteristic gnawing and pricking pain in the vulva, in two instances accompanied by a discharge; in all there were shrinkage of the vulva, leukoplakia and constriction of the introitus. Radical vulvectomy was done in the first three cases and extirpation of the labia in the fourth. The first patient died a year later from complicating cancer, in the next two the symptoms disappeared, and in the fourth they persisted possibly because of the patient's diabetes and the less radical operation. The third patient was given after-treatment with injections of estrogenic substance, in all 80,000 mouse units.

Norsk Magasin for Lægevidenskapen, Oslo

99:961-1064 (Sept.) 1938

*Stenosis in Aqueduct of Sylvius from Anatomic Point of View. B. Dahl and F. Harbitz.—p. 961.

*Treatment of Internal Hydrocephalus with Permanent Drainage of Third Ventricle. R. Ingebrigtsen.—p. 976.

Treatment of Gallstones at Naval Hospital from 1919 to 1937. K. Haugseth.—p. 989.

*Observations and Symptoms in Temporal and Occipital Tumors. A. Torkildsen.—p. 996.

Rare Hereditary Anomaly of Pigmentation. H. Sundfgr.—p. 1015.

Stenosis in Aqueduct of Sylvius.—In the first of Dahl and Harbitz's patients, a man aged 26 with general cerebral symptoms for a year, the diagnosis at necropsy was chronic leptomeningitis, ependymitis granularis and internal hydrocephalus. Examination showed pronounced proliferation of the neuroglia, especially in the third ventricle and about the

aqueduct of Sylvius, which was nearly obliterated, a slight inflammation in the choroid plexus and scattered perivascular cell infiltrations about the base of the ventricle system. An inflammation is considered the primary process. In the second patient, a man aged 59 with diffuse cerebral symptoms for three or four years, and marked internal hydrocephalus, an edematous cushion of neuroglia tissue obliterated the aqueduct of Sylvius. There was proliferation of the neuroglia and ependyma, with edema, softening and cystic degeneration. The first, second and third ventricles were dilated. A primary gliomatosis (incipient syringomyelia?) was indicated, especially about the aqueduct of Sylvius, and the atrophy of the medulla oblongata pointed to congenital structural changes as the main cause. In the third patient, a man aged 21 with massive internal hydrocephalus in the first, second and third ventricles for five years, there was ependymitis granularis in the ventricles, with gliomatosis and cystic degeneration around the aqueduct of Sylvius, and stenosis of the aqueduct. In the last patient, a girl aged 14 also with massive internal hydrocephalus, chronic leptomeningo-encephalitis was established, with secondary stenosis of the aqueduct of Sylvius. The hydrocephalus is ascribed partly to the stenosis, partly to the inflammation.

Internal Hydrocephalus.—Ingebrigtsen says that internal hydrocephalus is a frequent result of tumors in the third ventricle and of all tumors in the posterior fissure of the brain. In his patient, a man aged 26, a Nélaton catheter No. 8 was introduced through the aqueduct of Sylvius to the third ventricle; its upper end rested in the base of the ventricle, the lower end was passed through the fourth ventricle to the subarachnoid space. The patient became able to work and continued so for more than three years. Four years after the intervention extreme distention of the side ventricles was seen, the tumor in the posterior portion of the third ventricle, originally revealed by ventriculography as a small constant shadow, was now considerably larger, and the inner opening of the drain tube was surrounded by tumor tissue. On puncture of the side ventricles 192 cc. of clear fluid was removed from the right side, 132 cc. from the left side. The patient died in coma. The microscopic diagnosis was ependymoma. The consistency and appearance of the tube were as fresh as on its introduction. The author considers this method of drainage less dangerous than an opening of the base of the third ventricle, which contains the centers for a number of vegetative functions necessary for life. In the second patient, a girl aged 14, a tube was introduced through the aqueduct of Sylvius for permanent drainage of the third ventricle; she died five days later from bronchopneumonia. Immediately after the introduction of the drain tube in the first patient, paralysis of the rectus internus of the right eye occurred which completely receded; in the second case there was somewhat more grave paralysis of the eye muscles.

Temporal and Occipital Tumors.—Torkildsen analyzes the seventeen cases of tumor in the temporal lobe and nine of tumor in the occipital lobe of his 154 cases of verified tumors of the brain. The patients were mostly adults; the youngest was 13, the oldest 56. The most important subjective symptoms were, in order, headache, vomiting and, in the patients with occipital tumor, visual disturbances and in those with temporal tumor, focal epilepsy. Mental disturbances in eleven of the first group and seven of the second were seldom noted by the patients with occipital tumor, oftener by those with temporal tumor. All the patients with occipital tumor except one, who was blind, had defects in the visual field, but only two realized the fact. The change first appeared in the lower quadrant. Homonymous hemianopic changes are not recorded in the patients with temporal tumor. Sensory changes were rare. Motor deficiency symptoms were not infrequent in the patients with temporal tumor. Cerebellar dysfunction was frequently present, especially in the patients with occipital tumor. In the patient with aphasia, alexia and apraxia the tumor was mainly in the right hemisphere. Calcium atrophy on the same side as the tumor was established in two cases of temporal tumor, distention of the porus acusticus on the same side as the tumor in one case, and intracerebral calcification corresponding to the site of the tumor in one case. In the cerebrospinal fluid the albumin content was increased; the cell count was not over 16/3.

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DUODENAL ULCER

THE VALUE OF THE ROENTGENOLOGIC
DEMONSTRATION OF CRATER

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Present day apparatus and technic have increased the frequency with which the crater of a duodenal ulcer can be demonstrated. Many investigators still feel that duodenal deformity is sufficient for the diagnosis of ulcer and make no attempt to determine the absence or presence of crater. The demonstration of crater not only establishes activity but, as in the case of gastric ulcer, is useful in following the healing during a course of medical treatment.

DEFORMITY

Deformity of the duodenal bulb is an indirect sign that may occasionally result from extraneous influences,¹ may not be demonstrable even in the presence of a rather large crater, gives no objective clue as to the presence of active or healed ulcer and may decrease, remain stationary or increase, with resulting stenosis, during a course of medical treatment. In rare instances the deformity may be caused by adhesions or invasion of the duodenum by neoplasm. It is also claimed that spasm induced by extraneous stimuli may cause bulb deformity. Primary diverticula of the first portion of the duodenum are so rare that they need not be considered in a differential diagnosis. At necropsy healed duodenal ulcer with deformity is a frequent observation.² We have occasionally seen the typical purse string deformity in the routine examination of patients with pernicious anemia done to rule out gastric neoplasm. These patients, although giving no present history of ulcer, frequently admitted to ulcer-like symptoms at some time in the past. These "healed" ulcers were diagnosed by observing the evidence of a scar as indicated by fold radiation from a center, retraction and shortening of the bulb, formation of the "ulcer diverticula" and absence of a niche. However, with

healed ulcer radiating folds can be entirely absent and the form of the duodenum appear normal.³

Since bulb deformity may be caused by contraction of scar tissue, by mucosal swelling, by muscle spasm or by any combination of the three, it seems obvious that changes in the degree of deformity are not dependable evidence as to the healing of an ulcer. To judge and compare the amount of deformity present at different examinations is extremely difficult. During healing no appreciable change in the bulb deformity took place in the majority of our cases. When the degree of deformity did change, decrease was more frequent than increase. With a few exceptions, our cases bear out the statement of White,⁴ who said: "Thus far we have not seen a single markedly deformed cap which has filled out to its smooth, plump contour after treatment. Evidently a small amount of scar tissue or adhesions has persisted which still deforms the delicate walls of the duodenum." The deformity accompanying fresh ulcer and resulting from a spastic-pulling-in of the margins of the bulb will not become permanent unless contraction of scar tissue occurs.

HISTORY

In 1909 Barclay⁵ first described a persistent collection of barium as evidence of a duodenal ulcer. Haudek⁶ in 1911 established that certain persistent collections of bismuth in the duodenal bulb represented ulcer craters. This "bismuth fleck," or "niche sign," was thought to be a rarity until 1921, when Åckerlund⁷ published his first paper on the subject, based on a combination of fluoroscopic examination and filming.

In 1926 H. H. Berg,³ who had improved Åckerlund's technic by developing "gezielteaufnahme," or "aimed exposures," published his classic monograph on the diagnosis of duodenal ulcer. He reemphasized the importance of the direct signs and described craters and their accompanying mucosal patterns, carefully checking this work against pathologic material. Berg pointed out that radiologic observations of the crater and mucosal patterns allow one to study duodenal ulcer repeatedly during treatment, whereas the surgeon and the pathologist see the lesions only at a single stage.

ANATOMIC APPEARANCE OF CRATER

During the period when the conventional surgical treatment for duodenal ulcer was gastro-enterostomy without exposure of the inside of the bulb, little pathologic material became available for direct comparison with the roentgenologic appearances. With the advent of massive gastric and duodenal resections, pathologists

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1. Barclay, A. E.: *The Digestive Tract*, London, Cambridge University Press, 1933. Kirklin, B. R.: *Ann. Int. Med.* 9: 436-443 (Oct.) 1935.

2. (a) Portis, S. A., and Jaffé, R. H.: *A Study of Peptic Ulcer Based on Necropsy Records*, J. A. M. A. 110: 6-13 (Jan. 1) 1938. (b) Crohn, B. B.; Weiskopf, Samuel, and Aschner, F. W.: *The Life Cycle of Peptic Ulcer*, Arch. Int. Med. 35: 405-422 (April) 1925.

(c) Stewart, M. J.: *Brit. M. J.* 2: 955 (Nov. 24), 1164 (Dec. 16) 1922.

3. Berg, H. H.: *Ergebn. d. med. Strahlenforsch.* 2: 249-350, 1926.

4. White, F. W.: *M. Clin. North America* 2: 1431 (March) 1919.

5. Barclay, A. E.: *Brit. M. J.* 2: 549 (Aug.) 1910.

6. Haudek, M.: *Med. Klin.* 8: 181-184 and 224-229, 1912.

7. Åckerlund, Åke: *Acta radiol., Suppl.* 1. 1921.

and roentgenologists were able to study the specimens and accurately compare them with the roentgenologic appearances.

Judd⁸ classified ulcers into two types: (a) small superficial erosions not accompanied by palpable induration but surrounded by diffusely inflamed mucosa, which he termed duodenitis, and (b) deep ulcers, characterized by a definite crater and indurated margin.

Superficial Ulcers.—Puhl,⁹ working with excised tissue, found that superficial ulcers were as frequent as deep ulcers. He stated that flat ulcers are more or less round or oval and are accompanied by radial spurs. These spurs are formed in part by the erosion and in part by the distortion of the muscular wall. The neighboring mucosa may be thick and cross hatched, may form a high wall about the crater and may contain

microscopically from erosions as they involve the muscularis propria as well as the mucosa and submucosa.⁹ In resected surgical specimens Clairmont¹⁰ found that duodenal ulcers are more irregular than gastric ulcers and that linear craters are rare. The crater lies at the mouth of the scar tissue pocket, if present, at the center of fold radiation. It is usually found on either the anterior or the posterior wall, whereas scar tissue pockets (ulcer diverticula) are frequent on the greater and lesser curvatures of the bulb.¹¹

Multiple Craters.—Multiple craters and ulcer scars are frequently found at pathologic examination. In a series of ninety-two surgical cases of duodenal ulcer, Clairmont found multiple ulcers in fifty-four. That multiple ulcers may be overlooked on gross examination of the specimen was indicated by Gruber.¹² He stated that the reaction about an acute ulcer can be so great that it may be difficult to tell microscopically whether a second ulcer exists.

Berg³ has thus summed up the relationship between the pathologic and the roentgenologic appearances:

In the earliest stages of duodenal ulcer there are almost no reactive processes in the mucosa about the crater. Later, one encounters varying degrees of mucosal swelling, infiltration, connective tissue induration and, in chronic cases, involvement of the deep structures. The deep crater and rolled-up margin of a callous ulcer are easy to demonstrate, but in ulcers confined to the superficial mucosa the crater may be so shallow that it is quite impossible to demonstrate it roentgenologically in the living subject.

ROENTGENOLOGIC CHARACTERISTICS OF CRATER

Images of the bulb obtained with compression technique differ markedly from those obtained when pressure is not used. In the normal bulb fine longitudinal or spiral folds that converge at the apex are frequently found. Occasionally the pattern is cross hatched or polypoid, particularly when the organ is filmed in a partially contracted phase, and at the center of a peristaltic wave all folds become parallel. It is easier to obtain adequate patterns in pathologic bulbs than in normal bulbs. The explanation presumably lies in the inflammatory stiffening of the mucosa and submucosa.

Superficial Craters.—Since superficial ulcers not accompanied by reactive processes in the adjacent mucosa are too shallow to retain enough barium, they are rarely diagnosed roentgenologically. This fact may partially explain those cases in which there are typical symptoms of ulcer but neither roentgenologic nor gastroscopic evidence of ulcer. We have obtained a series of films, made under varying degrees of compression, in cases in which the bulb filled normally, which show faint, persistent, rounded, localized collections of barium that always recurred in the same location and were not accompanied by any demonstrable mucosal reaction. The rapid disappearance of the collection with the patient under medical management left grave doubt that a shallow erosion actually existed. In the accompanying table these cases are included under the heading active untreated, normal, because of our uncertainty as to the actual existence of a crater.

With a shallow erosion accompanied by reactive processes in the adjacent mucosa without permanent bulb deformity, the bulb is irritable and never fills com-

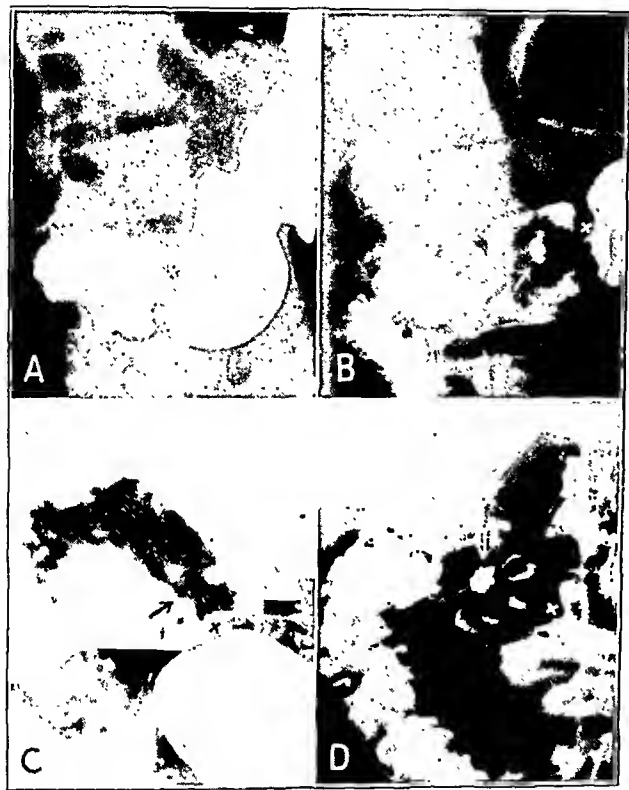


Fig. 1.—A, a well filled undeformed duodenal bulb. The indentation on the anterior border was inconstant at fluoroscopic examination. B, the same bulb after application of moderate compression. Note the central collection of barium (crater) surrounded by the translucent ring (inflammatory margin). C, a filled deformed bulb with a faint crater lying at the center of the deformity. D, the bulb shown in C after application of pressure. The faint irregular crater seen in C is more prominent. The streaks radiating from the crater represent barium sulfate between folds. The arrows indicate the craters and the pylorus.

numerous other erosions. Some pathologists believe that these lesions by producing edema, infiltration and scar tissue lead eventually to deformity of the duodenal bulb. Konjetzny and Puhl said that deep ulcers regularly develop from shallow ones, but Schindler, as a result of endoscopic studies on gastric ulcers, disagreed. We believe that shallow ulcers do produce the clinical picture of ulcer and do respond to ulcer treatment. Though we consider the question still unsettled, for the sake of convenience we prefer to look on duodenitis as a type of duodenal ulcer.

Deep Ulcers.—Deep ulcers may appear similar to the deeper erosions and may only be differentiated

8. Judd, E. S.: *Journal-Lancet* 41: 215-220 (April 15) 1921.
9. Puhl, H.: *Deutsche Ztschr. f. Chir.* 207: 202-247, 1927.

10. Clairmont, P.: *Würzb. Abhandl. u. d. Gesamtgeb. d. prakt. Med.* 21: 1-59, 1924.

11. Moynihan, B. G. A.: *Duodenal Ulcer*, Philadelphia, W. B. Saunders Company, 1910. Harding, D. B.: *South. M. J.* 23: 513-517 (June) 1930. Puhl,⁹ Clairmont.¹⁰

12. Gruber, G. B.: *Wien. klin. Wchnschr.* 38: 1253-1256 (Nov. 19) 1288-1290 (Nov. 26) 1925.

pletely. The margins are fuzzy, and the mucosal pattern has a peculiar cross hatched pattern without definite crater. There is accompanying gastric hyperperistalsis.¹³ In other cases in which there is clinical evidence of active ulcer there is a permanent bulb deformity without demonstrable crater. Whether these are cases of advanced duodenitis or cases in which there is a deep crater that cannot be identified, we do not know.

Deep Craters.—The deep ulcer crater is seen sometimes "full face" and sometimes "profile." Cole¹⁴ said:

In some instances the ulcer is viewed in profile so that one sees its indurated edges projecting into the intestinal lumen and its crater filled with bismuth. Retention of this "bullet hole" pocket may be differentiated from pouching and from normal accumulations in the cap. In another location the bullet hole may be observed "full face" through a distorted cap or bulb.

In the full face, or axial, view, usually seen with the patient in the right anterior-oblique position, the niche generally presents a dense, sharply defined, spherical, angular to linear collection of barium lying at the center of a deformity or at the mouth of a scar tissue pocket. The niche frequently is surrounded by a clear area,

Summary of 963 Cases of Uncomplicated Duodenal Ulcer in Which Examination Was Performed with Various Compression Techniques

Clinical Status	Roentgenologic Observations					Total
	No Constant Deformity					
	Deformity		Without Crater			
	With Crater	Without Crater	With Crater	Duodenitis	Normal Condition	
Active untreated*	389	225	105	10	42	899
Typical.....	389	225	105			
Atypical.....	25	6	7	0	7	45
Active treated.....	14	24	0	0	41	109
Inactive.....	31	102	0	0		
Total.....	431	357	112	10	53	963

* Typical indicates definite clinical evidence of active ulcer. Atypical indicates indefinite clinical evidence but adequate response to therapy. The ultimate diagnosis depended in a large measure on the roentgenologic appearances.

† For explanation of these cases, see text.

the inflammatory margin (fig. 1 A and B). In the healing phases or in the chronic stages radiating folds may appear about the crater (fig. 1 C and D) and persist after the ulcer heals. In rare cases the fleck in the crater of a deep ulcer will be so dense that it shows through the shadow of the barium-filled bulb.

In the profile view, most often obtained with the patient in the left anterior-oblique position, the crater projects from either the anterior or the posterior wall, resembling a gastric ulcer. The mouth of the crater is indented on both sides, and if sufficient compression is used the crater may be separated from the rest of the bulb by a band of decreased density. This zone of decreased density corresponds to the rolled-up margin of the crater seen in cross section. Occasionally the base of the crater is somewhat irregular, suggesting that in addition to barium it contains granulation tissue or debris.

To the anatomist, surgeon or pathologist, the various parts of the first portion of the duodenum (the duodenal bulb) are identified not so much by their geometric position relative to the frontal plane of the body as by their relationship to certain blood vessels and to neighboring structures. These workers are able to identify lesser curvature, greater curvature, anterior wall

and posterior wall even though peculiarities of build or other factors have displaced the bulb from its typical relationship to the frontal plane.

This is by no means true of the radiologist. Under ideal conditions, with the patient in the full frontal or full lateral position, the parts of the bulb described by the radiologist as lesser curvature, greater curvature, anterior wall or posterior wall correspond quite well with the actual anatomy of the organ. Under adverse conditions, however, when interpretation must be based on films made with the patient in an oblique position or when the bulb is displaced from its normal position, agreement is apt to be poor. Failure to recognize this fact has led to confusion in the past. For example, Åckerlund in his earlier papers reported that ulcers may project upward from what he took to be the short-

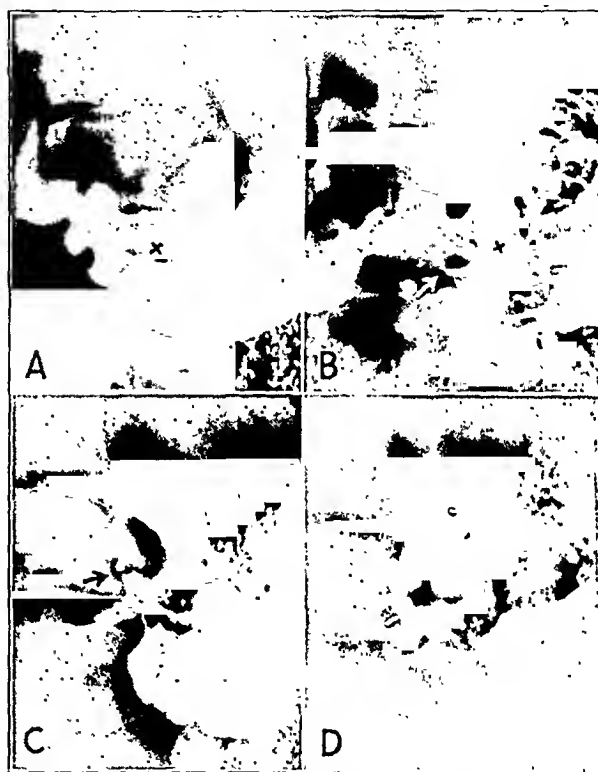


Fig. 2.—A, characteristic ulcer deformity in the duodenal bulb. B, the ulcer after application of pressure, showing the ring pattern near the base of the bulb. C, another ulcer, with a similar but smaller ring shadow. D, the ulcer shown in C after ten days of treatment. Note the characteristic niche at the location occupied by the ring shadow (see fig. 3).

ened and straightened lesser curvature of the duodenal bulb. Clairmont,¹⁰ studying excised tissue, felt that most duodenal ulcers were located on the anterior or posterior wall of the bulb. In later papers, based on compression films, Åckerlund agreed with Clairmont that most ulcers do occur on the anterior or posterior wall of the bulb rather than on its lesser or greater curvature. Sometimes a crater on the anterior or posterior wall may be brought into profile merely by manual displacement of the bulb, and films made after such manipulation might be misinterpreted as showing a crater on the lesser or greater curvature of the bulb.

The crater is usually located within the first 2 or 3 cm. of the duodenum, midway between the curvatures. Occasionally it is seen at the apex of the bulb or in the second portion of the duodenum.

13. Kirklin, R. R.: *Radiology* 12: 377-381 (May) 1929.
14. Cole, L. G.: *Lancet* 1: 1239-1244 (May 2) 1914.

Multiple Craters.—Multiple craters can be recognized but not with the frequency reported by pathologists. Berg recognized multiple duodenal ulcer craters or scars in one-half his cases. We have not been able to approach his percentage. In the axial views these craters, which fulfil all the described characteristics, may overlap each other or be entirely separate. Under manipulation they may change relationship to one another, indicating that one lies on the anterior wall and the other on the posterior wall. In the profile views they may be seen protruding one from the anterior and the other from the posterior wall.

CAUSES FOR MISIDENTIFICATION AND FAILURE TO FIND CRATER

Theoretically it should be possible to demonstrate a crater in 100 per cent of cases of active duodenal ulcer. Actually this is not the case. Reviews of the literature indicate a wide variation in the percentages of crater demonstrated by various workers. Accurate statistics on the demonstration of crater are difficult to obtain. Persons who as a routine use fluoroscopic examination combined with compression films made under fluoroscopic control demonstrate the crater in a higher number of cases of active ulcer than those using fluoroscopic examination alone or combined with films made without fluoroscopically controlled compression. The advocates of compression¹⁵ argue that the certain changes in the bulb are often too insignificant to be detected by fluoroscopic examination. The critics of compression¹⁶ contend that many collections of barium, though not really signifying a crater, cannot be differentiated from a crater. Åckerlund has emphasized the importance of technic and experience in such work. Berg, who has warned against overenthusiasm, points out that if there is frequent misinterpretation of crater-like shadows the method will suffer discredit. Hickey¹⁷ stated that the method requires a relearning of the art of interpreting films, with a new conception of the normal.

In view of these criticisms and warnings, it is necessary that persons who search for craters be familiar with the causes of "false craters," the differentiation of false from true craters, and some of the reasons for not finding craters actually present.

Spurious Craters.—Spurious craters may result from barium caught in pockets formed by contraction of scar tissue; clumps of barium caught between folds, lying loose on the mucosa or lying in an overlapping second and third portion of the duodenum; and barium held in a narrowed pyloric canal or in the canal of a contracted bulb apex when these structures are seen in an axial projection. Berg has described gallstones which, when projected over the bulb, appear as craters. We have seen such a phenomenon with kidney stones. Slight rotation of the patient made differentiation easy.

The spurious crater is more easily differentiated from the true crater at fluoroscopic examination. The ulcer crater is constant, even though the bulb is allowed to fill and undergo compression several times, whereas the false crater rarely reappears at the same place and in the same shape on several successive trials. It is extremely rare to see a crater protruding from the

greater or lesser curvature of the bulb near the base. This is an important point in the differential diagnosis of crater from scar tissue pockets, tongue-like processes or other collections of barium which frequently occupy these regions.

In identifying the profile views of the crater, the examiner must keep in mind that in the optimum positions, especially in the left anterior-oblique, pockets or even the lateral recesses of the obliquely placed bulb may appear as protrusions from either wall of the bulb. The profile of the crater, seen in the left anterior-oblique position, undergoes axial visualization when turned through 90 degrees into the right anterior-oblique position.



Fig. 3.—A, pathologic specimen of duodenal ulcer showing lymphogranulomatous tissue protruding upward from base of crater. B, the specimen after application of a thin layer of barium paste over the surface. The shadow of the lymphogranulomatous tissue is separated from the rolled-up margin of the crater by a ring of barium. C, a cross section taken through the ulcer, showing lymphogranulomatous tissue which has invaded all the layers of the duodenum. The ring pattern was produced by barium lying in the grooves (arrows) between the lymphogranulomatous plug and the margins of the ulcer.

Failure to Identify Crater.—Failure to demonstrate a typical ulcer crater does not rule out the possibility of active ulcer. The crater may be filled with deposits of mucus, a blood clot, food debris or granulation tissue, leaving no room for barium. In such cases the crater may not show until the bulb has been filled and wiped clean several times. This fact should be kept in mind in evaluating a roentgenologic report to the effect that no duodenal ulcer is present. A careless or overworked examiner may pass as normal bulbs in which an ulcer crater could eventually have been demonstrated if he had had time and patience to manipulate the bulb sufficiently to dislodge mucus and other detritus, thus allowing the crater to fill with barium.

15. Åckerlund, Åke: *Am. J. Surg.* 11: 233-259 (Nov.) 1931. Bowman, P. G.: *Compression Technic in Gastrointestinal Roentgen Diagnosis*, J. A. M. A. 94: 464-468 (Feb. 15) 1930. Berg.²
16. Buckstein, Jacob: *Am. J. Digest. Dis. & Nutrition* 1: 516-520 (Sept.) 1934. Kirklin, B. R., and Burch, H. A.: *Ann. Int. Med.* 9: 436-443 (Oct.) 1935.
17. Hickey, P. M., in discussion on Bowman.¹⁵

Forssell¹⁸ has observed ulcer craters in which the mouth is occluded by local swelling or by puckering of the mucosa as a result of muscular contraction. Both he and Geyman¹⁹ stated that some types of acute ulcers show no spot of greater density, being represented merely by an oval polyp-like negative pattern varying from 1 to 4 cm. in diameter. Such a pattern is evidently caused by swelling about the occluded mouth of the crater. A crater invisible at first sometimes appears after a short period of medical management, presumably because treatment decreased mucosal swelling or muscular contraction, allowing barium to enter the crater.

Berg stated that it is difficult or impossible to find the niche of a bleeding ulcer, as the loss of fluid results in a marked decrease or absence of the mucosal swelling that is often so prominent. It may have been this apparent disappearance of crater that caused Crohn and his associates² to state that hemorrhaging ulcers tend to heal rapidly. Our experience indicates that the time for healing varies as much with these ulcers as with those without hemorrhage. None of our patients were examined immediately after hemorrhage, which probably accounts for the fact that we have not had a perforation which could be directly or indirectly attributed to the use of compression.

We have seen a negative center in a duodenal ulcer crater in a few examinations on living subjects (fig. 2 *A* and *B*) and once in material obtained at autopsy. In some cases this shadow represents the granulation tissue plugs described by Mann.²⁰ We have not observed the shadow in the course of healing duodenal ulcer in human beings. In those cases in which the translucent center disappears after manipulation, it is presumably caused by food, a blood clot or debris (fig. 2 *C* and *D*). Berg has noted the end of a thrombosed artery projecting up from the floor in a case of gastric ulcer, and presumably the same thing could occur with duodenal ulcer. In the case studied at autopsy masses of lymphomatous glands were observed adhering to the duodenal bulb. An ulcer in the posterior wall of the bulb had eroded deeply, and masses of glands protruded up from the floor of the crater. Postmortem films made after the mucosa and crater were smeared with barium paste showed a frank negative shadow within the crater of the ulcer (fig. 3).

In several cases there were multiple translucent areas in the center of an ulcer crater. When first seen, one of these craters presented the conventional dense center. Nine days after the institution of treatment the center of the crater became mottled, but at subsequent examinations it was again uniformly dense (fig. 4). The cause of this mottling was not determined.

Infrequently a crater that is not seen with the patient standing appears when he lies prone or supine. In the prone position pressure may be exerted by inserting a translucent pad between the epigastrium and the surface of the roentgenoscopic table. Conversely, some craters seen with the patient standing may not be demonstrable in the other two positions.

FREQUENCY AND IMPORTANCE OF THE DEMONSTRATION OF CRATER

The accompanying table is a summary of the roentgenologic appearances in 963 cases of uncomplicated duodenal ulcer studied by us in the last four years.

In fifty-three cases the bulb was termed normal, having no demonstrable deformity or crater. There was no evidence of a lesion of the stomach at gastroscopic or roentgenologic examinations. In the four cases under the heading inactive, radiating folds were seen on compression. The patients had suggestive histories of ulcer or of definite hemorrhage in the past. In the forty-nine remaining cases the clinician diagnosed active ulcer because of pronounced clinical evidence. Seven of the patients subject to rigid medical management were examined several weeks after hemorrhage. It is possible that in their cases a duodenal or gastric ulcer had healed without leaving any roentgenologic or gastroscopic trace.

In 105 of the 109 cases in which there was no clinical evidence of active ulcer, the bulb was deformed. In three of these cases the roentgenologist thought that



Fig. 4.—*A*, large irregular crater surrounded by a wide inflammatory margin in an undeformed bulb. *B*, the same crater nine days later. Note the mottling and indistinct margins of the crater and the radiating folds. *C*, the formation after fourteen days of treatment. The crater and the radiating folds are more prominent, but the margins of the crater remain indistinct. *D*, the area six months after treatment was started. In the region previously occupied by the crater is an indistinct collection of barium. This pattern may represent lumen in the depression of an epithelized crater. The patient was symptom free.

there was definite crater as well. It is possible that these may have been cases of active ulcer with very atypical clinical evidence. Even if the roentgenologist was mistaken in his identification of crater, the percentage of error is only 0.3.

The demonstration of crater is of particular importance in diagnosing ulcer when bulb deformity is not demonstrable and in establishing activity in many of the cases in which the clinical symptoms and signs are not typical of ulcer. George²¹ has stated that ulcer is not present if no deformity is present. This is probably true if the shallow erosions are excluded. Any crater penetrating into the submucosa or deeper should be seen in profile as a bulb deformity if the factors which prevent ulcer crater from filling are absent. In

18. Forssell, G., in discussion on Brastrup: *Acta radiol.* 3: 217-220, 1924.

19. Geyman, M. J.: *Am. J. Roentgenol.* 28: 211-222 (Aug.) 1932.

20. Mann, T. C.: *J. Clin. North America* 5: 753-775 (June) 1925.

21. George, A. W., and Gerber, I.: *Am. J. Roentgenol.* 1: 257-293 (May) 1914.

112, or 14.2 per cent, of the 858 cases in which there was a history of active ulcer, crater was seen but bulb deformity could not be demonstrated in the antero-posterior or right oblique position. Occasionally, however, with the left anterior-oblique position the niche could be demonstrated in profile as an outpocketing, from either the anterior or the posterior wall. In other cases the bulb was so obscured by the stomach or by the second portion of the duodenum that the profile view could not be obtained. The duration of ulcer pain varied from twenty-five years to two weeks, with exacerbations of from nine months to ten days. In only thirty-six had symptoms begun as recently as six months before. Here, then, is duodenal ulcer with chronic symptoms but without demonstrable bulb deformity, a condition which, according to Garland,²² probably does not exist.

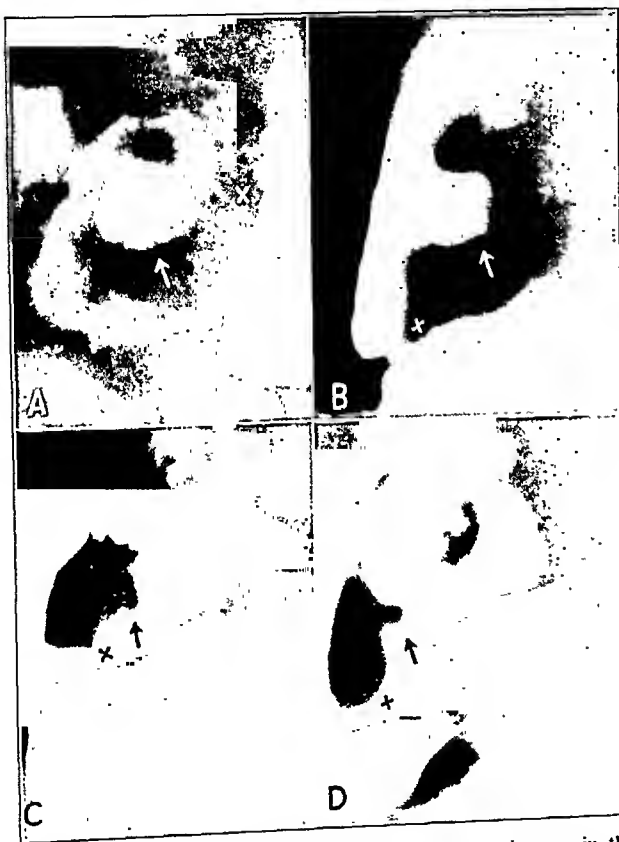


Fig. 5.—A, a large crater with its inflammatory margin seen in the axial projection a patient prone in the procedure. The film was made with the patient in the antero-oblique position. B, the same crater in profile projecting from the posterior wall. C and D, the same crater seen in profile sixteen days after treatment was begun. It had decreased both in depth and in diameter. Note the change in appearance as shown by the two views. The films were made within a few seconds of each other, the position of the patient remaining unchanged.

In thirty-eight cases the clinical symptoms and signs were not typical of ulcer. Crater was seen in twenty-five of thirty-one cases with deformity. In the other seven cases crater was present without demonstrable deformity. In most of these cases the identity of the crater was further established by its repeated demonstration in subsequent examination and by its gradual diminution in size during therapy. In such cases the crater is the only definite roentgenologic evidence of active ulcer. Irritability of the bulb as shown by alternating contraction and relaxation with rapid emptying is said to indicate activity of an ulcer.¹³ Åckerlund

stated that it is not a dependable sign. It might be argued that irritability alone is evidence of inflammation, but similar irritability in the stomach apparently is not evidence of gastritis.²³ Also, definite craters not accompanied by irritability occur in the bulb.

THE HEALING ULCER

Anatomic Changes.—The superficial ulcer usually heals rapidly without leaving any gross evidence of its existence. As to deep ulcer, the base becomes clean, coats over with fibrin and fills with granulation tissue or blood clot. The edematous margin decreases rapidly in height, and the mucosal edge progresses toward the center of the crater. These processes cause the ulcer to become shallower and to decrease in diameter. As healing progresses the central plug of tissue may project above the surface of the mucosa,²⁰ or the epithelium may grow down from glands of the adjacent mucosa to cover the granulation tissue of the base.²⁰ Radiating folds may appear, indicating the formation of scar tissue,²¹ with resulting fixation of the muscularis mucosae to the deeper layers.²⁵

Roentgenologic Changes.—Under adequate medical treatment the shallow crater may disappear so rapidly that, since no scar persists to indicate the previous existence of ulceration, it seems doubtful that a fleck of barium really represented a crater.²⁶ In the earlier stages the rapid decrease in the edematous margin of the deeper ulcer causes the niche to diminish rapidly in depth and to a less extent in diameter. The margin becomes less sharply defined when seen axially, and funnel shaped, with the base toward the mucosa, when seen in profile. Later the crater also decreases in diameter. If the patient adheres to his treatment, the crater may disappear entirely. Some craters seem to reach a point at which they become stationary, the margins fading off to merge with surrounding shadows (fig. 4). In such cases either the crater remains unhealed for a long period or its base epithelizes, with a resulting depression. Clairmont and Haudek showed that healed ulcer could be presented as a niche. Berg, however, had not seen this in a large amount of material. Radiating folds may appear or become more prominent.

A comparison of the roentgenologic and gastroscopic methods of examination has revealed that gastric ulcer may be very small but not completely healed when the niche disappears.²³ If this is true it may be postulated that disappearance of a niche does not necessarily indicate complete healing in the case of duodenal ulcer. The decrease in size probably indicates a favorable response to therapy.²³

The fact that some ulcers decrease or heal without the usual clinical treatment,²⁷ and the change in form that occurs in some ulcers during a single observation, preclude the placing of too much reliance on the roentgenologic evidence of healing in judging between various types of treatment.

A recent case in which we were able to view duodenal ulcer in profile seems to uphold the changeability of ulcer during one examination. At the first examination a 25 mm. ulcer (measured on the film) was seen axially and in profile extending from the posterior wall. We

23. Templeton, F. E., and Schindler, R.: *Am. J. Roentgenol.*, to be published.

24. Clark, D. M., and Geyman, M. J.: *Roentgen Evidence of Healing in Duodenal Ulcer*, J. A. M. A. 102: 107-112 (Jan. 13) 1934.

25. Portis and Jaffe.²⁴ Clairmont.¹⁰

26. Berg, H. H.: *Röntgenuntersuchungen am Innenrelief des Verdauungskamals*, Leipzig, Georg Thieme, 1930.

27. Kalk, H.: *Klin. Wchnschr.* 2: 1310-1312 (July 9) 1923.

felt that it had penetrated into the pancreas because of its size and position. In ten days it had decreased considerably in depth. In two sets of profile films taken within a few seconds of one another the ulcer seemed to change in diameter and depth with the contraction of the bulb. Seven days later the patient was again examined. Although the crater had continued to decrease in size, this time in diameter as well as depth, a distinct variation was seen in the crater, which seemed associated with contraction of the bulb. As contraction of the bulb began, the crater seemed to become deeper and narrower, and films of these changes were made (fig. 5). Three days later the patient died of coronary occlusion. At necropsy the ulcer was large and shallow and lay on the posterior wall. Its appearance did not correspond with the roentgen appearance. This was to be expected, as exact correlation of a crater with the roentgen picture can be obtained only by the immediate fixation, preferably by freezing, of the tissue removed by resection.²⁸ This fixation prevents the rapid loss of surrounding edema and the effect of muscle tone. In this case, however, the absence of any penetration into the pancreas and of any marked amount of adhesions or induration on the serosal surface was noteworthy. This changeability may indicate the absence of marked induration.

COMMENT

The best clinical evidence of activity and healing is the roentgenologic demonstration and the progressive and complete disappearance of the crater.²⁸ Our observations confirm the observations of others²⁹ that a large percentage of niches persist for a considerable time after symptoms are clinically relieved. In one case the existence of a persistent crater, refractory to medical treatment, was proved at postmortem examination. In another case, in which recurrent clinical evidence of ulcer was lacking, the roentgenologic evidence of crater was confirmed at operation. The recurrence of ulcers in the same place, confirmed by gastroscopic examination in the case of gastric ulcer, appeared also to occur in the case of duodenal ulcer. Our evidence strongly suggests that absence of pain and of occult blood from the stool is not in itself necessarily a definite criterion for healing, although it is a favorable sign.

CONCLUSIONS

1. By using proper roentgenologic technic, ulcer crater can be demonstrated in a high percentage of cases of active involvement. This demonstration is of great value in differentiating active from inactive ulcer and in diagnosing ulcer when bulb deformity is absent and the history atypical.
2. Demonstration of a crater is of definite significance in both treatment and prognosis. The ulcer crater seen at roentgen examination indicates that the ulcer has penetrated into the submucosa or into the deeper muscular layers; consequently the danger of hemorrhage or acute perforation is great. Absence of pain is not in itself a definite criterion of healing, for many patients under management may be symptom free even though a large niche is present.
3. Healing cannot be said to be complete until long after the crater has disappeared.

950 East Fifty-Ninth Street.

ABSTRACT OF DISCUSSION

DR. THEODORE L. ALTHAUSEN, San Francisco. This is an excellent summary of the new technic of examination for duodenal ulcer. I am convinced of the value of this technic, since eight years ago I was privileged to spend a year in the medical institute at Leipzig, Germany, where Dr. Schatzki (a pupil of Berg's who originated it) was using this method, which essentially involves the giving of smaller amounts of barium sulfate, the employment of controlled compression, and the use of a snapshot attachment on the fluoroscope. In this country the roentgenologists have been rather slow in adopting the technic. I think for two reasons: In the first place, it is not easy. Even an expert roentgenologist usually has to have some training with some one who is familiar with the technic. In the second place, there has been little demand for this method of examination on the part of clinicians who have been satisfied with a clinical picture suggesting duodenal ulcer, combined with the demonstration of a deformity of the duodenal bulb by the roentgenologist. The authors should be congratulated on their excellent x-ray films. I think we all could appreciate even the finer points that were made, which is rather unusual in lantern slides of x-ray films.

DR. FREDERIC E. TEMPLETON, Chicago: There is one point I wish to make. At the University of Chicago we attempt to bring out on the films all lesions that we see at fluoroscopic examination. It is not at all frequent, but not too infrequent, that we are able to gain a lead as to the presence of a crater on the films and then go back and find it at fluoroscopic examination. Sometimes the crater is seen only on the films. Our percentages of crater demonstration, around 65, are very conservative; if we are not sure of a crater, we do not attempt to stretch the point too far.

FASCIAL ADHESIONS IN PAIN
LOW IN THE BACK AND
ARTHRITIS

CHARLES MURRAY GRATZ, M.D.

NEW YORK

Fascial planes function as joints synchronizing motion between muscles, groups of muscles, nerves and blood vessels. Traumatic and inflammatory lesions may involve these planes, resulting in myosynovitis or fascial adhesions. These are believed to be competent producing causes of muscular pain by involvement of the nerves and of limitation of the normal range of motion in the joint by retardation of the gliding mechanism of the muscles. A diminished power of repair of lesions involving the lower part of the back may be caused by arthritis if this term applies to the fascial as well as to the osseous joints. This paper deals with lesions involving primarily the soft tissues, and lesions involving the spinal column and its contents are therefore presumed to be excluded.

Biomechanical studies of fibrous tissues have been coordinated with gross and histologic studies of anatomy, with roentgenograms and finally with histologic sections. The therapeutic application of the aforementioned concepts to fascial surgery, with case reports, is included.

Since the entire work depends on the study of joints in relation to human locomotion, a definition may be

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From the Department of Surgery, Division of Orthopedics, New York Post-Graduate Medical School and Hospital, Columbia University, and New York City Hospital.

Dr. Arthur Steindler, George Hawley and Plato Schwartz, surgeons who are pioneers in studying human locomotion, have cooperated with me for many years. Miss Willoughby Holmwood and Miss Genevieve Hunter assisted.

²⁸ Ettinger, Alice, and Davis, W. E.: *Am. J. Digest. Dis. & Nutrition* 1: 579-581 (Oct.) 1934. ²⁹ Porfiss and Jaffé; ³⁰ Crohn, Weiskopf and Aschner; ³¹ Berg; ³² Buckstein.
²⁹ Walko, K.: *Mitt. a. d. Grenzgeb. d. Med. u. Chir.* 39: 1-44, 1926.
³⁰ Berg; ³¹ Ackerlund; ³² Clark and Geyman; ³³ Ettinger and Davis.

in order. With apologies to Webster, a joint may be described as a space functionally designed for motion. This definition includes osseous joints, the tendon moving in its sheath and the fascial spaces functioning as joints. Lesions involving primarily the osseous skeleton are not discussed in this paper. The ease and accuracy of x-ray studies of bones may account for the relatively small amount of clinical attention given to fibrous tissues. The fibrous tissues transmit stresses between the component parts of the locomotor apparatus and protect the nerves, blood vessels and lymphatics as they traverse the fascial joints. The spinal

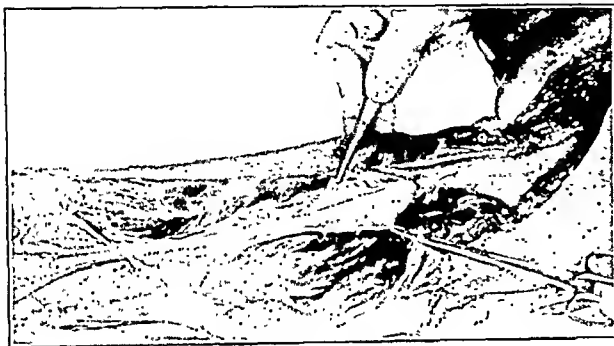


Fig. 1.—Fascial covering divided.

column similarly supports the body and protects the spinal cord and its structures. The osseous joints are protected by the ligaments and other fibrous structures surrounding them. The fascial joints, with their important contents, are protected in locomotion not only by the muscles but also by the tensile strength of the fibers of the fascial planes.

Research workers at Columbia University have presented determinations of the relative tensile properties of mammalian fibrous tissues. These data showed a comparative similarity of the ligaments and tendons to the fibers of the fascial planes. Preliminary studies of the effect of shearing stresses on fibrous tissues were included in the clinical application to fascial surgery. Traumatic lesions resulting in shear frequently are the cause of serious disability in the lower part of the back.

An etiologic diagnosis explaining the cause of obscure muscular pain has been one of surgery's major problems. The use of a contrast medium has added to the roentgenographic accuracy of diagnosis in the study of lesions involving the central nervous system and the lungs. A similar surgical and roentgenographic technic of diagnosis is suggested for lesions involving the fascial planes. The fact that many patients afflicted with obscure muscular pain are gravitating into the hands of irregular treaters of symptoms shows the urgency of solving this major economic and industrial problem. It is believed that an accurate method of first localizing the pathologic change may lead to hope of surgical correction.

The anatomic studies were similar to those of Kanavel and the late Dr. Prentiss of Iowa. Photographic studies were obtained by air insufflation. The fascial covering of the sciatic nerve was found to be insufflated with air though the planes were injected remote from the nerve. The sciatic nerve resembles a tendon in its tendon sheath (fig. 1). In some subjects the fascial covering of the nerve was adherent (fig. 2). When adhesions were dissected, the anatomic picture resembled a tendon after an acute infection. My associates and I were thus enabled to demonstrate

anatomically the presence of adhesions involving the lining of the fascial space and the structures it encloses. It is not difficult to visualize the effect of such adhesions in locomotion. They are believed to be a competent producing cause of radicular muscular pain.

The same mediums and the method of insufflation were used clinically for roentgenographic study. Pneumofasciograms were thus made in a manner paralleling the surgical and roentgenographic technic of pneumocephalograms and studies of the thorax. Air in the fascial planes of relatively normal patients is evenly distributed (fig. 3). In the fascial planes of arthritic patients the air has an irregular distribution (fig. 4) and has been so reported.¹ The variation between the two forms of distribution is believed to be due to fascial pathologic change.

Biopsies of animal and human fasciae enabled us to study and present histopathologic data. The fascial fibers are normally covered with mesothelial cells of an origin similar to that of the cells lining the osseous joints and the pleural cavity. They apparently line closed spaces; otherwise the air would not be retained in the fascial spaces after injection.

The histologic and histopathologic work was done in association and is being published with Dr. L. H. Meeker. Figures 5 and 6 have been reviewed by Drs. Ward J. MacNeal and Arthur Purdy Stout and finally by Dr. Arthur Steindler. Histologically the lesions are shown by altered secretions, by "thickening of the opposing fascial surfaces or by actual adhesions."² The synovial covering of the muscles is frequently involved, and the lesion may then be known as myosynovitis. In the opinion of Dr. Steindler, degenerative processes such as those seen in the illustrations are probably accompanied by changes and weakening of the tensile properties of the fascial fibers themselves. Preliminary data obtained at autopsy were reviewed, and changes in the tensile properties were noted. One woman 72 years of age, invalided for many years, died of myocarditis, and we tested her tissues the day of death. They showed markedly diminished tensile



Fig. 2.—Dissection of adhesions.

strength, and the physiologic range of elasticity was practically nonexistent. Similar changes were noted in a leg amputated for endarteritis obliterans and in a leg amputated for malignant change after roentgen therapy. Only one series of test data from an arthritic patient is as yet available. The aforementioned concepts are of particular interest when correlated with the discussion of rest and may indicate the extreme care necessary when surgical intervention is deemed advisable.

1. Gratz, Charles Murray: Air Injection of the Fascial Spaces: A New Method of Soft Tissue Roentgenography, *Am. J. Roentgenol.* 35: 750 (June) 1936.
2. Gratz, Charles Murray, and Meeker, L. H.: The Role of Fascia in Myosynovitis, to be published.

THERAPEUTIC APPLICATIONS

The first of five conclusions of an article published in 1928³ was "The treatment of a patient with arthritis should be based on a complete history and physical examination, supplemented by all indicated laboratory



Fig. 3.—Even distribution of air in the fascial planes of a normal patient.

work." In 1929 there was completed a thorough study from the orthopedic standpoint of over 200 patients. In a review of their cases it was found that the medical work-up was as important as the orthopedic; hence nothing worthy of reporting was found. A study of carefully selected private patients was then begun, and it was on such patients that the air insufflations were later used. They were treated in close cooperation with their family physician, and certain of them are included in series A.

In the past ten years the principles of biologic engineering have clarified our surgical procedures, and a thorough medical examination of the patient is standard routine. Roentgenograms of the bones and cultures of the stools are a requisite to any therapy.

The correlation of human locomotion with the clinical problems is in order. In human biologic development the upright position necessitates an increased tension on the posterior group of muscles and nerves and increases the tensile and shearing stresses on the lower portion of the back. The existence of the "posterior division syndrome" and the fundamental biochemical changes necessitated by biped locomotion have recently been reported by Steindler.⁴ The increasing sedentary habits of bipeds are in effect a second new deal, and recessions could be expected. The fascial joints in the lower part of the back and surrounding the sciatic

nerve are apparently, like some of the bipeds themselves, "on the spot." The individual "spots" have been localized and studied by Steindler. Rheumatic lesions involving such traumatized areas are increasingly difficult to treat as the sitting-down habit keeps increasing.

Anatomic proof of fascial adhesions was found in the region of the body recently designed for sitting. The locations which we selected independently for surgical insufflation correspond to those affected by the posterior division syndrome of Steindler.

The synchronized approach to the study of defects in human locomotion permits application to the problem of pain low in the back. One must first decide whether to increase or diminish the patient's activity. To patients with an adequate physical reserve and muscular pain alone, postural exercise, walking and training of the muscles may be of real clinical value. Postural training may realign osseous structures, thus reducing shear phenomena in the functioning of dependent mesodermic structures. The patients treated by insufflation and operation were selected from those for whom an increased range of motion was desired.

For patients with acute symptoms and diminished physical reserve, rest is frequently advised. They may be admitted to the hospital immediately and kept in bed twenty-four hours a day during the time of examination. Carefully fitted supports, usually braces, are used before they are allowed to resume gradually the upright position. The fibrous tissues protecting the nerves are weakened by traumatic or infective processes, necessitating rest. Rest allows them to regain physiologic strength. Clinical judgment alone sets the dividing line between activity and rest. I am thoroughly in accord with Dr. Reginald Burbank's belief that exercise is beneficial provided pain does not per-



Fig. 4.—Irregular distribution of air in the fascial planes of an arthritic patient.

sist after the motion has stopped. I strive to have each patient establish his own tolerance to pain. When determinations of the normal safety factor of human tissues are established, greater accuracy will be permitted.

When rest in bed is advised a primitively hard bed is, with few exceptions, used. The patient is agreeably surprised at the resulting comfort. The knees are frequently flexed and the lumbar region of the back sup-

3. Gratz, Charles Murray; Wright, Irving Sherwood, and Mackenzie, Inn: Arthritis: Medical and Surgical Treatment, S. Clin. North America 8: 443 (April) 1928.

4. Steindler, Arthur, and Luck, J. V.: Differential Diagnosis of Pain Low in the Back, J. A. M. A. 110: 106 (Jan. 8) 1938.

ported. Light traction on the leg may be in order. These measures relieve the tension of the posterior group. The therapeutic value of rest includes that of casts, of operation on soft tissues and of surgical rest of joints by arthrodesis. These procedures have been reviewed in a previous publication.⁵ It may be pertinent, however, to say that any operation on osseous structures necessitates dissection of soft tissue and is



Fig. 5.—The mesothelial covering of fascial fibers.

followed by a prolonged rest. The value of these two factors may equal that of the curative operation on the bones. Arthrodesis has a valuable role, but I am now discussing only those cases in which the primary pathologic change is believed to be in the soft tissues.

With the cooperation of G. B. Karelitz, professor of mechanical engineering, Columbia University, equipment is being devised to make use of engineering advances for the comfort and physiologic rest of bedridden patients.

The role of heat, training of the muscles and manipulations is of interest. These measures reached a high degree of perfection in the Roman civilization and are still being used. Penetrating heat in the form of local or general hyperpyrexia is probably a real advance. It is believed that heat causes an increased secretion in the fascial joints which may in selected cases result in improved function and resulting diminution of symptoms. "Moreover there is reason to believe that the temporary success in some of these cases by massage and manipulation may be explained by the releasing of secretion, the freeing of agglutinated surfaces or by breaking of adhesions, rather than by changing the anatomical position of osseous structures."² Theoretically and practically such measures may prove of clinical value in cases in which an increased range of motion is desired. They are included in the post-operative treatment of patients who have undergone insufflation. If the fascial adhesions are weaker than the nerves and blood vessels traversing the fascial joints, their release may prove beneficial. In cases of acute involvement the adhesions are probably nature's method of protecting weakened joints and as such may be stronger than the nerves and blood vessels themselves. Manipulation may then result in the disastrous tearing of nerves and blood vessels. The fortunate as well as the most unfortunate results of manipulation

are believed to be so caused. Dr. Melvin Henderson stressed the need of approaching manipulative procedures with the same care that is used in approaching open operative corrections, if not even greater care. I use manipulative therapy and insufflation with exactly the same precautions. In all cases the patient is treated first, his symptoms are treated later and an individual program based on the result of study is outlined.

The residual group of patients who have not responded satisfactorily to any of the forms of treatment mentioned are now the major problem. Fascial disease of sufficient degree to warrant surgical insufflation or operative correction is accompanied by a definite limitation of motion. Roentgenographic localization of the fascial change precedes any operative correction.

REPORT OF CASES

Not only do insufflation and operative procedures free mechanically the fascial adhesions, but the oxygen in the air may have a definite therapeutic effect on the synovial covering of the fascial fibers. This effect is occasionally noted in thoracic and peritoneal therapy. There is little therapeutic value in freeing adhesions without first removing their cause. The patients included in series A are consecutive private patients, are all members of the residual group previously referred to and were all treated for therapeutic as well as diagnostic purposes. This series is believed worthy of a few comments. The first patient was treated by insufflation March 16, 1935, and has remained symptom free since the completion of the therapy. A patient with traumatic pain low in the back complicated by arthritis was treated by insufflation in June 1935 and has been symptom free since that time. The word cure is never used either to the patient or in reports.



Fig. 6.—High power plantar fascia in case 1 of series D. Note hypertrophy of the mesothelial cells.

For twenty-three of forty-one patients satisfactory improvement is reported. They have (1) an increased range of motion of their involved joints, (2) a definite diminution in or freedom from symptoms and (3) an increase in their useful activity. They have been observed or have reported after an accurate follow-up. For fifteen patients of series A satisfactory improve-

5. Gratz, Charles Murray: *Biochemical Studies of Fibrous Tissues Applied to Fascial Surgery*, Arch. Surg. 34: 461 (March) 1937. Gratz, Wright and Mackenzie.³

ment of questionable duration is reported because of an incomplete follow-up. The treatment of the remaining three patients is considered a failure even though a temporary improvement followed insufflation.

Series B consists of nineteen patients from New York City Hospital reported on through the courtesy of Drs. Lyman Weeks Crossman, David Sloane and George J. Plehm. Most of them were treated for diagnostic purposes only. The series includes patients with advanced arthritic contracture following the use of a cast, with progressive muscular dystrophy and with postoperative gas bacillus infection and one apparently normal person but is not reported in detail.

Series C consists of thirty-seven patients treated at various institutions, many for diagnostic purposes only. In certain of them spectacular relief of symptoms occurred. In some the relief has persisted for over two years. Their cases are not reported in detail.

Series D consists of four patients who underwent operation. Two are from series B (patients 3 and 4). Their cases are reported in some detail:

CASE 1.—A patient aged 56 underwent operation Oct. 27, 1936, for fascial adhesions and removal of a spur of the os calcis. Fascial biopsy showed myosynovitis. This patient has been symptom free and able to indulge in full activities up to the time of last examination, Oct. 18, 1938.

CASE 2.—A man aged 47 with a history of a tear in the lumbar fascia from the crest of the pelvis, arthritis and constipation which followed the swallowing of lye when he was a child, underwent an operation Nov. 30, 1937, for fascial adhesions at the attachment of the lumbar dorsal fascia to the ileum. Roentgenograms and histologic study of sections confirmed the diagnosis of fascial adhesions. At the time of the last examination, April 23, 1938, the patient had a normal range of motion of the back and no local pain at the operative site. The condition of his abdomen, however, warranted a thorough study of this region, and it is too early to estimate the final result.

CASE 3.—A patient aged 53 underwent operation Nov. 24, 1937, after a diagnosis was made of fascial adhesions causing limitation of motion of the knee. The adhesions were divided, a biopsy specimen was taken and the fascia lata was removed from the upper side of the incision and placed between the condyles of the knee. Traction instead of a cast was used postoperatively. Examination May 4, 1938, showed that the patient's activities had satisfactorily increased and that the range of motion of the knee as a result of both types of therapy had increased from about 10 degrees to over 35 degrees. There was no pain and no instability.

CASE 4.—A woman aged 41 underwent operation Nov. 10, 1937, after a diagnosis like that in case 3. The fascial adhesions were dissected, a biopsy specimen was obtained and Bennett lengthening of the quadriceps with a living suture from the tendon of the same muscle was performed. This patient has been followed to Oct. 18, 1938, and now has 45 degrees of painless motion of the knee operated on in contrast to 5 degrees of very painful motion when she first went under treatment.

The cases reported through the courtesy of my associates (series E, F and G in the table) are included and make a grand total of 398.

SUMMARY

The surgical and roentgenographic technic of air insufflation is being reported this winter in two chapters of a new book by Dr. John Russell Carty. Special equipment has been devised for the process⁶ and it is always done as a hospital procedure. The dangers of infection and embolism are great even though 398 cases are reported in which there were no complications.

Preliminary histologic work shows the need of studying fascial pathologic changes in the fasciae. If the lead of Dr. Herbert C. Clark of Panama and his associates Drs. Bates, Callender and Kelser could be followed and biopsies of the osseous and fascial tissues be included in routine postmortem examinations, much valuable information could be obtained. The concepts herein stated are merely an effort to increase the

Summary of 398 Cases of Pain Low in the Back in Which Air Insufflation Was Used

Location of Adhesions						
Area of Posterior Division Syndrome						
Upper Part of Back	Middle Part of Back	Lower Part of Back, Thighs	Knees	Feet	Total	
3	1	19	4	6	33	
Other Areas						
Hand and Forearm		Shoulder		Total		
5		5		10		
Series A						43
Private patients treated by air insufflation between March 16, 1935, and April 9, 1937, for both diagnostic and therapeutic reasons						
Result of treatment not relevant.....						2
(One patient, on whom insufflation was last performed July 28, 1935, died of unrelated causes several months later, with the parts treated in good condition; one underwent operation)						
Satisfactory improvement						23
(Increased range of motion and diminution of symptoms were definitely known)						
Satisfactory improvement of questionable duration.....						15
(The improvement was the same as in the preceding group, but the follow-up was not sufficiently accurate)						
Treatment a failure.....						3
(In two of these cases the condition was probably due to obesity, and in one it was probably a Marie Straumpell process)						
						43
Series B						19
Patients at New York City Hospital, many of whom underwent insufflation for diagnostic purposes only and two of whom were operated on later						
Series C						37
Patients treated at various institutions, many for diagnostic purposes only						
Series D						4
Patients who underwent operation, no complications or infections						
Series E						20
Patients of Dr. John Russell Carty of the New York Hospital, who underwent insufflation for diagnostic purposes only; no complications						
Series F						Over 75
Patients of Dr. Abel Peck of the Charles S. Wilson Memorial Hospital, Johnson City, N. Y. Dr. Peck: "I have been very much pleased with the air injection therapy in a group of selected cases."						
Series G						200
Patients of Dr. Millard C. Beyer, Akron Ohio. Dr. Beyer: ". . . without any untoward results."						
Total patients treated without complications.....						398

accuracy of examination of the soft tissues of the locomotor apparatus by the methods that have proved successful in studying other portions of the body:

1. Biologic engineering led to the discovery that the fascial planes of the human body function as joints.
 2. The clinical application of this fact led to a study of myosynovitis and fascial adhesions.
 3. Histopathologic studies confirmed the existence of fascial joints, myosynovitis and fascial adhesions.
 4. These adhesions are believed to explain radicular muscular pain.
 5. A coordination of all the studies led to a surgical and roentgenographic technic for the study of defects in the soft tissues of the locomotor apparatus.
 6. The clinical applications are believed to show that the method can be safely applied over a period of years.
- 30 East Fortieth Street.

6. Gratz, Charles Murray: A New Automatic Valve for Measuring Air Insufflations, J. Bone & Joint Surg. 19: 835 (July) 1937.

ABSTRACT OF DISCUSSION

DR. M. C. BEYER, Akron, Ohio: A few years ago I began to inject air into fascial planes for therapy. Not having at my disposal laboratories equipped for research work, I depended on Dr. Gratz for information with regard to histopathology on this subject. I want to emphasize the fact that the cause of arthritis is not known and that the same factor which causes changes in bone may cause changes in soft tissue. It is difficult to treat these changes from the etiologic standpoint because the etiology is not known. So the symptoms are still treated. I treat symptoms by means of air injection. I find that in many cases of low back pain, when insufflations of air are made and roentgenograms are taken, definite bands of fibrous tissue are seen. I find that a normal person who can bend over and touch his toes and create an arch in his back does not exhibit fibrous adhesions in the roentgenogram. Patients with so-called lumbago were given insufflations of air, which finds its way under the lumbar fascia, and later during the process of massage to break up adhesions crepitus is elicited. I massage until the crepitus disappears. I feel, but I may be mistaken, that the crepitus is caused by the breaking up of fibrous adhesions between the muscle body and the sheath of the muscle. I give treatment and get the best results in the acute cases, the so-called cases of lumbago. A man who does heavy labor, lifting a tremendous weight, frequently will bend over to tie his shoe and will suddenly be caught with a sharp pain in his back. The patient often can be greatly benefited by insufflation of a quantity of air and then massage of the air. The muscle is loosened up so that the man stands up straight and is able to bend over and touch his toes without any pain. That effect is lasting in the majority of cases. I have given injections in well over 350 cases, and in my locality approximately 700 injections have been made without any untoward results.

DR. DAVID R. TELSON, Brooklyn: What happens when the perfectly well man stoops over to pick up a collar button, gets a terrific pain in his back, and comes up crooked? There are two explanations. The first is that the sacro-iliac joint slips. The second is that for some reason the muscle itself undergoes a sudden spasm. I believe in the second explanation, with Dr. Gratz, that abnormal adhesions exist between the fascia and the muscle. One little adhesion tears and sends the whole muscle into spasm. Why doesn't one think it is the joint? I have operated on sacro-iliac joints under local anesthesia. I have never been able to reproduce the pain shooting down a man's leg by doing anything to the sacro-iliac joint. I have been able to reproduce the pain by separating the fascia from the muscle either manually or by injecting air. At times when I put air into this fascia the man complains of exactly the same pain shooting down his leg. I do not believe that these pains can be traced on any definite nerve outline. If there is some disturbance within that muscle, the pain is relayed back to the spinal cord and then comes down to Head's area, the pathways of which one cannot trace any more than one can accurately trace a gallbladder pain referred to the back.

DR. J. ALBERT KEY, St. Louis. Apparently there is something to this injection of the fascia. I myself do not know how much. I do not know how many of these patients got better or how many would have got better if they had not had their fascia injected, but I do think that Dr. Gratz has been led astray by his pathologist and I do not believe that these spaces are lined by endothelium.

DR. CHARLES MURRAY GRATZ, New York: It is gratifying to know that many other surgeons are safely and successfully using these methods. I wish particularly to thank Dr. Beyer for his enthusiastic cooperation and to acknowledge with deep gratitude the privilege I have had of reporting the results of his studies. I wish also to thank Dr. Key for his discussion of the pathologic work shown. The existence of fascial joints and the pathologic involvement of them is the corner-stone of our entire approach to the study of low back pain and arthritis. The existence of fascial joints has been proved to the satisfaction of both the medical and the engineering professions. Anatomic and radiologic work over a period of more than

three years has proved that these joints are air tight by the fact that the insufflated air remains in them. The pathologic studies have been reviewed and approved by the three eminent pathologists previously mentioned and are the foundation of the clinical work. I have purposely waited since 1935 in reporting the successful treatment of arthritic patients by fascial surgery until there has been a complete agreement of all my colleagues on the etiologic diagnosis on which the treatment is based. Hence, Dr. Key, I will not take any chance of creating an incident which might develop into a major conflict. Certain patients suffering from fascial adhesions may be successfully treated by air insufflations alone with very dramatic results. A conservative method, however, is to keep the cart behind rather than in front of the horse and use air insufflations with radiographic studies to localize the pathologic condition and permit an operative correction in selected cases. In the operative cases here reported fascial adhesions have been localized, removed, studied pathologically and plastic operations on the soft tissues successfully done in the lower part of the back, the knees and the feet. It is believed that a new ray of hope based on sound biomechanical and surgical facts may now be extended to certain of these unfortunate individuals. In addition to my colleagues previously mentioned may I in conclusion thank Dr. S. N. Blackberg, Mr. Dan Everett Waid, Prof. G. B. Karelitz and Mr. R. L. Wegel, who gave unsparingly of their time and effort over many years to help build the foundation on which our present hopes are based.

THE INDUCTION OF SEXUAL MATURITY IN THE GENITALLY HYPO- PLASTIC ADULT

THROUGH THE USE OF TESTOSTERONE
PROPIONATE

H. S. RUBINSTEIN, M.D.

BALTIMORE

In a recent contribution Hamilton¹ reported that through the use of testosterone propionate a man aged 27 with migraine headaches was relieved "with some degree of success" of his hypogonadism, cryptorchidism, impotence, hot flushes and mental attitude. The failure to induce spermatogenesis in this case was explained by a statement to the effect that the male hormone like the extract from the urine of pregnancy was capable only of maintaining an already existing spermatogenesis. Cases such as those reported by Hamilton are relatively scarce. It appears worth while to record all carefully gathered data regarding such patients, particularly those treated, since relatively few patients have been subjected to treatments with synthetic androgens.

REPORT OF CASE

The following study, based on clinical and laboratory observations, is therefore considered to be timely:

History.—P. C., a white man aged 31, was referred for study in March 1936 because of infantile genitalia (fig. 1). His family and early personal histories were noncontributory. He first became aware of his defect at the age of 10 years when he noticed the difference in size between his and his playmates' genitals. A physician was consulted but the mother was advised that the child would "outgrow it." He was thin until he was 13 years of age, at which time a faint crinis pubis made its

From the Research Laboratory, Surgical Division, Sinai Hospital. The Ciba Pharmaceutical Products, Inc., cooperated by partially defraying the expense involved in this study and for supplying the testosterone propionate (perandren) used. Dr. A. E. Goldstein made the genito-urinary examination of this patient.
1. Hamilton, J. B.: Treatment of Sexual Underdevelopment with Synthetic Male Hormone Substance, *Endocrinology* 21: 649 (Sept.) 1937.

appearance. From then on he became progressively fatter. During adolescence he was made keenly aware of his "failing" by his chums, so that he began to brood about it and made many unsuccessful attempts to secure a cure.

The patient was 62½ inches (159 cm.) in height, weighing 164 pounds (74.4 Kg.). The measurement from the symphysis pubis to the bottom of the feet was 4½ inches (11 cm.) more than the measurement from the symphysis pubis to the top of the head. The fat was distributed over the pelvic and shoulder girdles, breasts, abdomen and trochanters. The legs showed a lateral curvature with moderate genu valgum and flat feet.

The skin was very smooth and the face beardless, although the axillae did show a few sparse hairs. The voice was high pitched. Examination of the mouth showed an absence of all third molars (unerupted) and rather small upper lateral incisors.

The genitalia were markedly underdeveloped. The pubic escutcheon was sparse, with the apex directed distally. The penis was 2 cm. in length and only about 1 cm. in diameter (about 3 cm. in circumference). There was no evidence of hypospadias; the prepuce was partially removed by circumcision. Both testes were present within the scrotum but were only about the size of a pigeon egg. The epididymides were small and the prostate and seminal vesicles were not palpable. Neurologic examination was negative but a mental survey disclosed that he was very much concerned over his defect not, as he put it, because he was "interested in girls" but rather because his acquaintances jibed him. There were many periods of sadness and on occasion crying spells. During these periods he suffered from anorexia, constipation, insomnia and preoccupation. He made friends easily, however, because of his affability. His intelligence was of the average adult type and his sensorium was clear for tests dealing with orientation, information, memory, calculation, reasoning, reading, writing and judgment. His record as a clerk was good, although he

Fröhlich configuration due to neurohypophysial involvement as evidenced by genital dystrophy, genu valgum and pes planus; (5) reactive depression with feelings of inferiority resulting from an awareness of his difference from others, the taunts of fellow workers and his own overemphasis of his plight.

The treatment as first instituted consisted of a diet of 90 Gm. of carbohydrate, 50 Gm. of protein and 60 Gm. of fat (1,100 calories); thyroid one-half grain (0.03 Gm.) three times a day; solution of posterior pituitary 1 cc. three times a week and extract of urine of pregnancy 300 rat units three times a week.

In addition, psychotherapy in the form of reeducation and encouragement was employed to counteract his feelings of inferiority and hopelessness. During the next five months there resulted a definite recession of fat, a growth of the penis to 5 cm. (fig. 2) and a suggestion of a prostate gland on palpation. In addition, the voice became slightly more husky. Treatment over the course of another year which included several short injection-free periods, however, failed to show added improvement.

For this reason in July 1937 injections of the synthetic androgen testosterone were begun and for a period of four months the patient was given 5 mg. of the propionic acid ester of this hormone ("Perandren"-Ciba) three times a week, a total of 250 mg. While penile growth occurred, it was not striking. In the latter part of October 1937, dosage was increased to 25 mg. three times a week. After a period of one week the genitalia began showing marked changes. The penis showed an increment of enlargement which was greater than that observed during any previous corresponding period, and erections were almost continuous. December 23 the penis measured 6.5 cm. when flaccid and 9 cm. when semirigid. The most striking change, however, was in the circumference of the organ, which had increased from an original measurement of 3 cm. to one of 9 cm.

At this time the patient stated that he had very recently become interested in a girl whom he intended to marry. He further stated that a test at coitus had resulted in the escape of seminal fluid. Although the possibility of a childless marriage was explained to the patient and his intended wife they were not deterred, so that during the month of January 1938 they were married.

Sexual relations were successfully carried out daily for one week after marriage and have been continued at a pace of three times a week for a period of two months. It is interesting that no treatment was given from January 6 to January 25 (nineteen days), during which time the sex pace was maintained, both patient and partner being gratified.

February 22 the penis, which was 7 cm. when flaccid, reached a size of 12 cm. in length and 10 cm. in circumference when rigid (fig. 3).

A condom specimen obtained at this time disclosed numerous spermatozoa, but all were motionless. From other studies on spermatogenesis² it was known that this immotility could have resulted from the chemicals associated with the condom. For this reason a masturbation specimen was obtained March 8. This revealed many motile but also a number of immotile spermatozoa. The prostate and seminal vesicles at this time were definitely palpable, although they were not very large.

Another specimen of the ejaculate obtained March 15 revealed a total volume of 0.6 cc. with a total sperm count of 8,400,000, a number corresponding to 14,000,000 per cubic centimeter.

2. Rubinstein, H. S.: The Effect of Anterior Pituitary-like Hormone on Spermatogenesis in the Human. *Endocrinology* 22:75 (July) 1938.

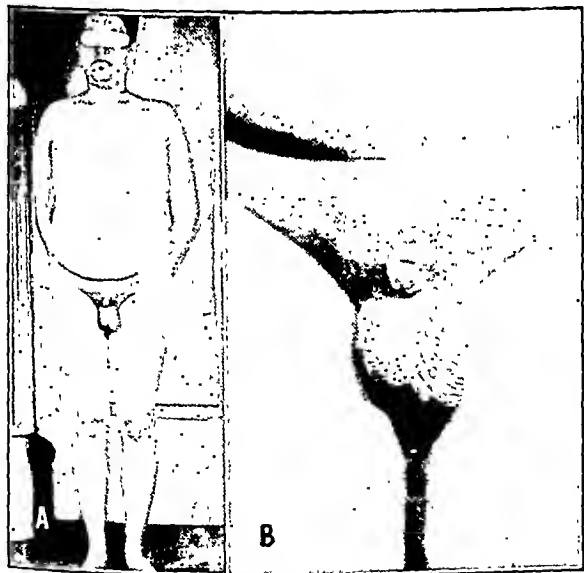


Fig. 1.—A, the patient March 29, 1936, before treatment. B, the genitalia March 29, 1936, before treatment, showing infantile dimensions of penis. The testes were the size of pigeon eggs.

had to leave several jobs because of the taunts of other clerks. Roentgenographic study was noncontributory, but the basal metabolic rate was minus 14 per cent.

The diagnosis was (1) hypopituitarism (hypobasophilism with deficiency of sex hormone and hypo-eosinophilism with growth defect); (2) hypothyroidism, secondary in character, with lowered basal metabolic rate and unerupted third molars; (3) hypogonadism (probably secondary) with infantile genitalia, feminine crinis, high pitched voice, beardlessness, eunuchoid skeletal proportions, small lateral incisors, and impalpable prostate and seminal vesicles; (4) dysplastic constitution with



Fig. 2.—The genitalia Oct. 4, 1936, after five months of treatment with gonadotropic substance from the urine of pregnancy (follutein). The penis is 5 cm. in length and is refractory at this time to further treatment with gonadotropic substance.

Viability was present, as already mentioned, and the majority of spermatozoa were of normal form. At present the patient is still under active treatment, receiving 25 mg. of testosterone twice a week.

Experimental Observations.—Since the patient displayed mature and motile spermatozoa following treatment with testosterone propionate, it became interesting to determine whether



Fig. 3.—*A*, the patient Dec. 23, 1937, after treatment. *B*, the genitals Dec. 23, 1937, after treatment with testosterone propionate (perandren), showing marked growth.

this hormone had actually initiated this phenomenon in an originally immature testis or had merely stimulated a rather dormant function in a testis already capable of sperm formation.

For this purpose a group of sexually immature rats (*Mus norvegicus* var. *albus*) of Wistar Institute strain were subjected to intraperitoneal injections of this substance. Treatment was begun at 20 days (weaning age) and a dose of 1 mg. daily

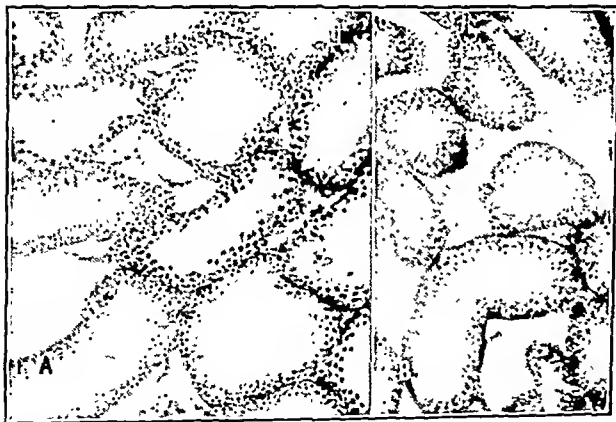


Fig. 4.—*A*, section taken from testis of an immature rat control. *B*, section taken from testis of an immature rat treated with testosterone propionate (perandren), showing thickened tubules but no increase in interstitial tissue.

(except Sunday) was given for a period of eleven days. The animals were killed twenty-four hours after the last injection, at which age spermatogenesis is still normally incomplete.

It was found that testicular descent occurred in the test animals four days after injections were begun, i.e. at 25 days of age, while the testes of the control rats did not descend until they were 32 days old.

In addition to earlier testicular descent, the genitalia of the test animals were grossly larger than those of the controls. Critical measurements, however, will be included in a detailed report of more extensive studies now under way. Microscopic examinations of the testes (fig. 4) showed a rather thickened tubular wall in the test animals as compared to the controls but no change in the interstitial elements. Mature spermatozoa were lacking in all animals but there was an increased proliferation of germinal cells as evidenced by mitotic figures, thickened tubular wall and the extrusion of immature cells (spermatocytes) into the epididymis (fig. 5).

COMMENT

It is interesting to note that the hormone used was capable of stimulating libido and of enlarging the hypoplastic genitalia of this patient to a stage at which marriage was possible, sex pace increased and marital relations satisfactorily maintained. In addition it stimulated the germinal epithelium of the testis so that ejaculation of live spermatozoa resulted. It is important to note, however, that this hormone did not bring about any change in hair distribution or beard growth.

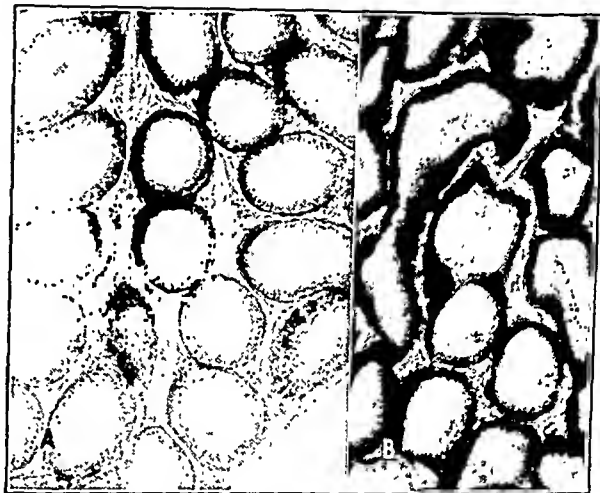


Fig. 5.—Section taken from epididymides from same animals shown in figure 4: *A*, from immature control showing empty tubular spaces; *B*, from immature test animal showing numerous premature spermatic forms in the tubular spaces.

This is noteworthy since many believe that the masculine crinis and bearded face result from the influence of the male sex hormone. In the light of recent experience, this causal relationship becomes questionable. As a matter of fact, the use of testosterone propionate in females³ fails to incite facial hair growth. In addition, an adult patient with testes bilaterally absent from the scrotum, now under observation, shaves every other day. What is actually responsible for hirsutism is still a matter of conjecture, but from clinical experience with adrenal tumors it appears that this gland is, in a measure, a contributor to this phenomenon.

So far as the spermatogenic effect of testosterone is concerned it is important to note that this hormone acts by stimulating proliferation of germinal epithelium. Thus immature animals when treated exhibit an outpouring of immature forms (spermatocytes) into the epididymis, and mature males, as will shortly be shown,⁴ react with an increase in the output of mature spermatozoa. It appears, therefore, that testosterone has the

3. Rubinstein, H. S., and Abarbanel, A. R.: The Use of Testosterone Propionate in the Treatment of Dysmenorrhea, *Am. J. Obst. & Gynec.*, to be published.

4. Rubinstein, H. S., and Kurland, A. A.: The Effect of Testosterone Propionate on Spermatogenesis in the Human, in preparation.

same effect on the germinal portion of the testis as does the pregnancy urine extract⁵ and castrate urine extract;⁶ i. e. it stimulates proliferation of the germinal epithelium in the stage of development at which the testis finds itself. It differs from these other hormones, however, in that it fails to stimulate the interstitial tissue.

Since mature spermatozoa were obtained in the case reported and since testosterone as shown by experiment merely stimulates proliferation of germinal cells to a stage at which the germinal cells can develop at the moment, it means that the testis in this particular patient had reached a stage at which it could react to this hormone by an increased output of spermatozoa. What stimulated the testis to a stage at which it could so react is unanswerable at this time. From experiments in the rat it is improbable that testosterone was immediately responsible but it is difficult to gainsay the secondary effects induced by the treatment which may have played a part in producing the final picture.

The preparation used, testosterone propionate, is the most active of all the known androgens, since it has been shown that an ester of testosterone is more active than the unattached molecule⁷ and that of all esters synthesized the propionate is most effective.⁸

Finally, it is important at this time to think of the testis as an organ consisting of two glands of internal secretion, (a) interstitial and (b) tubular. Since hormones fail to stimulate their own cells of origin,⁹ the stimulation of the tubular gland and the lack of effect on the interstitial gland lead one to assume that the synthetic testis hormone testosterone is identical with that androgen derived from the interstitial tissue.

SUMMARY AND CONCLUSION

A genitally hypoplastic man six months after cessation of response to treatment with gonadotropic substance from the urine of pregnancy was subjected to injections of testosterone propionate. This substance was injected intramuscularly in 5 mg. doses three times a week from the latter part of July to November 1937. Dosage was then increased to 25 mg. three times a week. In January 1938 the genital condition had become improved to such a degree that the patient married, cohabited and ejaculated live spermatozoa. While the voice became somewhat deeper, distribution of hair and the initial beardlessness remained unchanged.

Laboratory studies on the effect of this hormone on the testis disclosed a stimulation and proliferation of germinal epithelium but failed to reveal a hastening in maturation of the testes. It was concluded, therefore, that in this case secondary effects may have been responsible for first causing the germinal epithelium to reach such a stage of maturation and that further treatment with testosterone resulted in the proliferation and discharge of mature and live spermatozoa.

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5. Rubinstein, H. S., and Radman, H. M.: A Comparative Study of the Gross and Microscopic Effects of the Follicle Stimulating Hormone and Anterior Pituitary Sex Hormone on the Rat Testis, *Am. J. Physiol.* **122**: 319 (May) 1938.

6. Rubinstein, H. S.: The Effect of Castrate Urine Hormone on the Testis, *Endocrinology* **23**: 171 (Aug.) 1938.

7. Miescher, K.; Wettstein, A., and Tschopp, E.: The Activation of the Male Sex Hormones, *Biochem. J.* **30**: 1970, 1977 (Nov.) 1936.

8. Kochakian, C. D.: The Comparative Efficacy of Various Androgens as Determined by the Rat Assay Method, *Endocrinology* **22**: 181 (Feb.) 1938.

9. Loewe, S.: A Pharmacological Ejaculation Test for Bio-Assay of Male Sex Hormone, *Proc. Soc. Exper. Biol. & Med.* **37**: 483 (Dec.) 1937.

9. Collip, J. B.: Some Recent Advances in the Physiology of the Pituitary, *J. Mount Sinai Hosp.* **1**: 28 (May-June) 1934.

ELECTROTHERMIC COAGULATION OF AORTIC ANEURYSMS

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Observations of inactivity in saccular aneurysms completely filled with an organized blood clot have established the efficacy of "nature's cure." The principle of inserting wire into an aneurysm to induce clotting is basically sound.

The first attempt to inactivate an aneurysm by wiring is attributed to Moore in 1864.¹ Fifteen years later Corradi¹ suggested insulating the needle through which wire is passed into an aneurysm and connecting the protruding end of the wire to the positive pole of a battery, applying the negative electrode to the skin in the vicinity of the aneurysm. Application of from 50 to 100 milli-

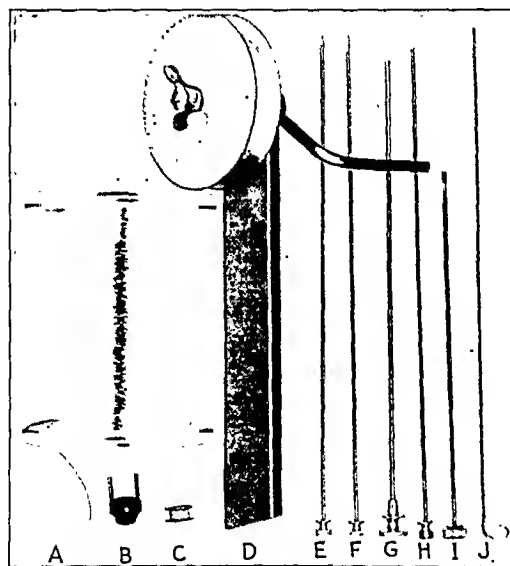


Fig. 1.—A, enameled wire on spool; B, electrode cap, adapted to H; C, self-retaining skin retractor; D, hand reel for winding wire on spools; E, a trocar pointed stylet adapted to G for traversing firm tissues and piercing the sac of the aneurysm; F, tapered blunt stylet adapted to G for traversing tissue of lung; G, 14 gage 6½ inch needle made of stainless steel, with the end beveled from without in; H, inner sheath for needle G, which locks in place and has the end beveled from within out, fitting exactly with needle G to furnish a rounded, nonabrasive end; I, wire passer adapted to H, and J, a blunt stylet adapted to H.

amperes resulted in the formation of an ionization product at the surface of the wire in contact with the blood. The wire generally used was a 29 gage wire of gold or silver alloy. This method of wiring aneurysms was most popular in America.

Colt¹ more recently devised and popularized in England a collapsible wire cage which could be introduced through a needle and expanded in the aneurysm.

Read at a section meeting of the American College of Physicians, New York, April 8, 1938.

From the Department of Surgery, Presbyterian Hospital, and the Department of Physiology, Columbia University College of Physicians and Surgeons.

A. R. Kemp and C. S. Fuller of the Bell Telephone Company helped to develop a suitable insulation for the wire. Prof. K. S. Cole of the Department of Physiology, Columbia University College of Physicians and Surgeons, and Mr. P. W. Spence of the Bell Telephone Laboratories advised and cooperated in the development of the electrical technique employed. Morris Eckman of the Department of Gas Therapy, Presbyterian Hospital, designed and constructed the reel. Frederick C. Wappler of the American Cystoscope Company designed and made the wire passer and needle. The wire was furnished by Baker & Co., Inc., of Newark, N. J.

1. Keen, W. W.: *Surgery: Its Principles and Practice*, Philadelphia, W. B. Saunders Company, 1921, vol. 5, pp. 216-349.

A thorough review of the literature led to the conclusion that the operation of wiring aneurysms as it has been performed fails to give satisfactory results. Relief of pain seemed consistent but rarely was maintained. A few aneurysms grew less rapidly. Occasionally a brilliant success resulted from the procedure. However, the results in most cases were discouraging.

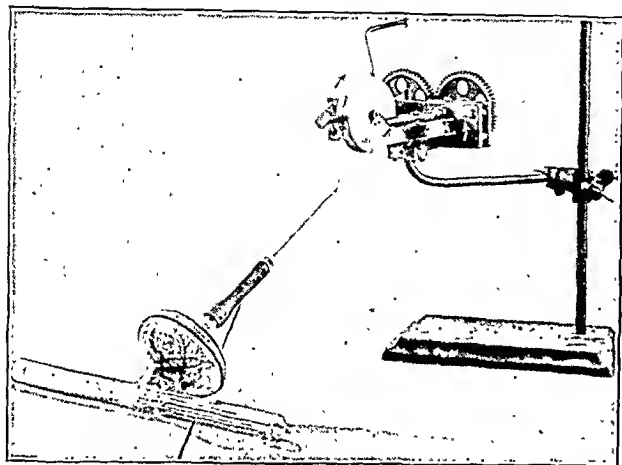


Fig. 2.—A geared reel which serves to rotate the spools in opposite directions as the wire is unwound. An aneurysm model with wire within. The wire passer is screwed into place on the needle.

Experimental and clinical studies convinced us that fast moving blood will not clot on wire. We found that the velocity of blood flow through saccular aneurysms of equal size varied as much as 300 per cent,

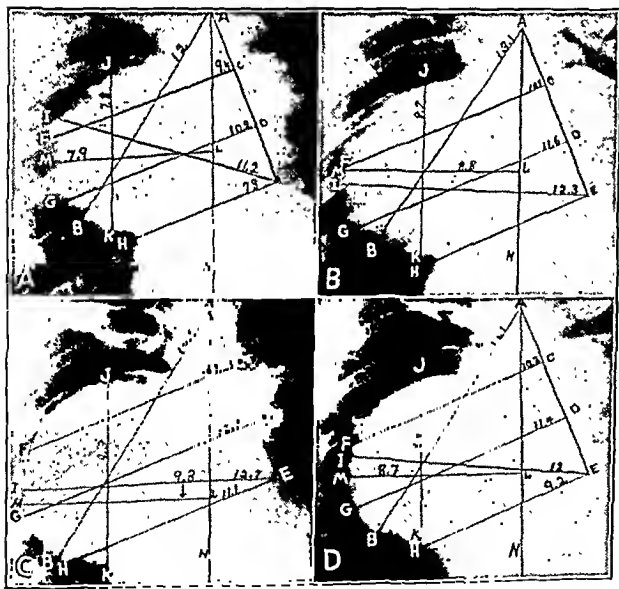


Fig. 3 (case 5).—View A was taken March 30, 1931; view B, Jan. 25, 1933; view C, Jan. 11, 1935, and view D, Feb. 20, 1936, eleven months after wiring and electrothermic coagulation. View D was taken after the injection of 20 cc. of diodrast into the aneurysm. Measurements: A-N, midline vertical; M-L, the farthest border of the aneurysm; A, posterior spine of the seventh cervical vertebra, and E, a point at the lateral edge of the thoracic aorta determined by a compass one leg of which is set at A, 13 cm. distance. With A-E as a base line, equidistant points C, D and E are taken, from which parallel lines C-F, D-G and E-H are projected to the lateral border of the aneurysm. A-B is the distance from A to the farthest edge of the aneurysm. E-I is the distance from E to the farthest edge of the aneurysm.

depending on the size of the opening into the sac. Former methods of wiring aneurysms afforded no index of blood velocity as a guide to the amount of wire necessary in a given case. It is probable that the

extremely variable results following the procedure may be explained on the basis of incomplete clotting.

We wish to present a method of wiring aneurysms in which the blood velocity, not the size of the aneurysm, indicates the amount of wire necessary to retard the rate of flow to a point at which complete mass clotting takes place. The results in eleven cases in which aneurysm of the aorta was operated on by this method are of sufficient interest to report in detail.

There is a general impression that aneurysms have become less common. Moore,² however, reported that nearly 100 per cent of the women and from 30 to 49 per cent of all patients with cardiovascular syphilis have no knowledge of the beginning or the presence of syphilis. This makes it seem likely that aneurysms will occur for many years to come.

During the twenty year period from 1917 to 1936 there were 456 patients with aneurysm admitted to the Presbyterian Hospital and Vanderbilt Clinic. Of the aneurysms, 397 (87 per cent) were of the aorta. There were 232 cases from 1917 to 1928 and 224 cases from 1927 to 1936.

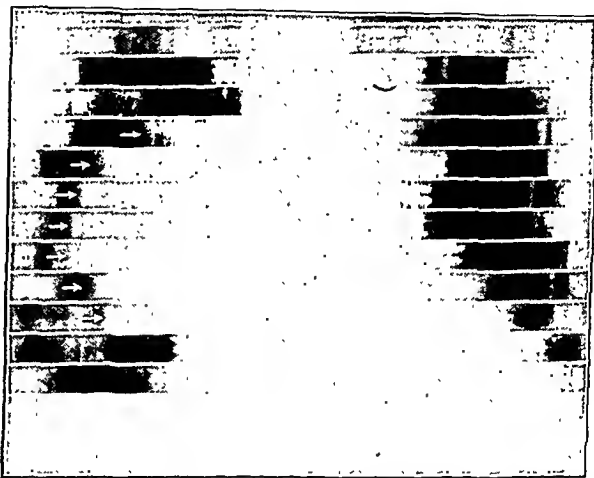


Fig. 4 (case 5).—Roentgenkymogram of the heart and saccular aneurysm of the ascending arch two years and two months after wiring. Note the absence of pulsation of the wall of the aneurysm (arrows).

It is reasonable to attribute to the Wassermann test and modern antisyphilitic therapy a great part in the prevention of aneurysms. Once the yellow elastic tissue of the aorta has been destroyed and the media so weakened by endarteritis, however, the resulting aneurysm introduces into the circulation a new and vicious mechanical factor. The wisdom of trying to eliminate the spirochete from the aneurysm cannot be denied. Conceding the benefits of bed rest, the unfortunate patient faces today the same old threats of sudden death by rupture, a lingering death by strangulation or acute distress from pressure symptoms. It is only necessary to compare these results with the occasional "nature's cure" seen at necropsy to appreciate the significance of complete clotting in arterial aneurysms.

In a study of sixty-one necropsy specimens of aneurysm of the aorta, complete clotting was noted in six (14 per cent) of the forty-two saccular aneurysms. Nineteen (25 per cent) of the sixty-one aneurysms were of the fusiform variety. In seven (37 per cent) of these, concentric clotting had narrowed the lumen available for blood flow to a diameter equal to or less than the

2. Moore, J. E.; Dangle, J. H., and Raesinger, John C.: Cardiovascular Syphilis, Arch. Int. Med. 49: 879-924 (June) 1932.

width of the aorta. This represents nature's cure. Rupture of the aneurysm had not occurred in a single case: death from some unrelated cause was the rule. The clotted specimens had every appearance of permanent inactivity. The patient usually had been free from symptoms attributable to the aneurysm.

The nutrition and strength of an aneurysmal sac depends largely on an outgrowth of collateral vessels about its neck. Blood, circulating under pressure, creates a strain on the wall of the sac varying with the square root of its surface area and, to a lesser extent, with the rate of the blood flow. Doubling the diameter of an aneurysm increases the strain on the sac 100 per cent. The stretched sac, further devitalized, is of course weakened. Thus there is a vicious circle in a rapidly growing aneurysm of increased strain on a wall of diminishing strength. Lowering the blood pressure by bed rest in such cases often prolongs and, no doubt, often saves life. The temporary reduction of blood pressure permits the strengthening processes within the sac an opportunity to become effective. Unless complete clotting takes place—and this rarely occurs—as the blood pressure rises, the aneurysm is again subjected to the vicious strain. In a clotted aneurysm, however, the physical laws governing solids obtain. Thus the strain on the sac of an unclotted sacular aneurysm multiplies with growth, whereas filling the sac of an aneurysm completely with a solid clot reduces the strain on the sac to that of the lateral wall pressure on the surface area of the mouth of the sac. In the case of fusiform aneurysms, narrowing the lumen to the diameter of the parent artery reduces the strain on the sac to that of the lateral wall pressure on any other equal segment of the parent artery.

It seemed likely that if a sacular aneurysm could, with certainty, be filled with a clot which was adherent to the wall of the sac, inactivation of the aneurysm and a reduction in its size might be expected to occur.

METHOD³

Inactivation of an aneurysm by clotting cannot be accomplished without bringing about two important conditions: (1) presence of an adequate clot-stimulating surface and (2) a sufficient reduction in the velocity of blood flow. Wire immersed in circulating blood, if heated to a temperature above the heat coagulation point of blood proteins, becomes coated with a protein coagulum which is difficult to scrape off. When introduced into an aneurysm in adequate amounts and heated it affords an excellent clot-stimulating surface of protein coagulum.

Wire introduced into an aneurysm offers an impediment to blood flow. If introduced in sufficient amounts it will slow the blood to a velocity at which, in the presence of an adequate clot-stimulating surface, complete mass clotting of the aneurysm takes place.

We have selected an alloy (silver 90 per cent, copper 10 per cent) which, when drawn into a 34 gage wire (Browne and Sharpe) has the proper electrical resistivity of heating. The small size of the wire, one half the size of that formerly used in wiring aneurysms, and its lack of spring make it safe to use in adequate amounts.

The wire is insulated with a thin coat of enamel. This makes it possible to heat it, after inserting it into an aneurysm, by connecting a battery of approximately 100 volts to the two protruding ends. Since the oper-

ator knows the temperature coefficient of resistivity of the wire, its temperature changes can be followed by bridge measurements (fig. 5). From the current values necessary to raise the temperature of the wire successively 5, 10 and 15 degrees (C.) above body temperature it is possible to determine the current necessary to raise the temperature of the wire to any desired level. The current required to heat the wire to a given temperature is dependent then on two factors: (1) distribution of the wire within the sac and (2) cooling of the wire, which is dependent on the velocity of the blood flow. In order to keep the electrical requirements within 100 volts and to facilitate better distribution of the wire within the aneurysmal sac, we have elected to insert and heat the wire in segments of 33 feet (10 meters).

A 33 foot segment is wound equally on two aluminum spools. The center of the wire is bent sharply in a loop that will pass through a special needle (fig. 1). The wire is autoclaved and its insulation tested. A 1 cm. incision is made under local anesthesia. A self-retaining skin retractor (fig. 1) is inserted. Deep injections of procaine hydrochloride are made, and the special needle is inserted into the aneurysm. The two aluminum spools are now mounted on a special reel (fig. 2). The loop of wire in the center of the 33 foot segment is passed through the wire passer, which for the time is left unattached to the needle within the aneurysm, and then through the needle into the aneurysm 2 cm. beyond the end of the needle. The operator holds one wire and advances the other, thus forcing the formation of the first loop of wire within the sac. A few loops of wire are introduced in this manner. The special wire passer is now screwed into place on the aneurysm needle (fig. 2) and the rest of the 33 foot segment of wire quickly passed, two wires at a time. With the wire passer it is possible to introduce a 33 foot segment of wire in about four minutes.

As the wire is unwound from the spools the gears of the reel turn so as to rotate the spools in opposite directions (fig. 2). This gives the wire, on reaching the aneurysm, a torque to the right and to the left, serving to separate the wire and distribute the loops within the sac. The ends of the wire are bared of insulation and anchored to the electrode cap, which attaches to the end of the needle (fig. 1). A roentgenogram of the aneurysm is taken at this point to confirm the distribution of the wire. Insulation of the wire is again tested, and, if it is satisfactory, the wire is heated, usually to an average temperature of 80 C., for from five to thirty seconds. Patients without general anesthesia usually experience some discomfort (never severe) while the current is on. After the first heating of the wire, it is reheated, and the diminished current required to heat it to the same temperature is noted. The wire is now clipped flush with the needle and the ends pushed into the sac.

Since the rate of cooling is the factor determining the current necessary to heat the wire distributed within the aneurysm, a good index of the velocity of blood flow through the aneurysm is obtained. For example, it may require twice as much current to heat a segment of wire in one sacular aneurysm as to do so in another having a smaller mouth. It follows then that the higher the amperage required to heat the wire, the greater will be the number of 33 foot segments necessary to impede the blood flow.

From the experimental and clinical development of this principle, there has been evolved for wiring aneu-

3. The experimental development of this method and a detailed description of the technic have been omitted for the sake of brevity. This material will be the subject of a subsequent article.

rysms an accurate method having several practical aspects. On the basis of the number of amperes of current required to heat the first 33 foot segment of wire, well distributed within an aneurysm, to 80 C., it is possible to determine (1) the variety of aneurysm, (2) approximately the amount of wire that will be necessary to impede the blood flow and (3) the occurrence of complete mass clotting of the aneurysm if a final segment of wire requires only from 3 to 4 amperes for heating to 80 C.

A 33 foot segment of wire has a surface area of 8 square inches, which is increased to 16 square inches after the deposit of the protein coagulum. The magnitude of the impedance of blood flow necessary becomes further apparent when we add that the wire in the eleven cases we are reporting averaged 118 feet.

Former methods of wiring aneurysms afforded no index of blood velocity as a guide to wiring. Wire was recommended which, because of its large size and stiffness, could not be safely used in amounts sufficient

for the more active aneurysms. This repetition has the added advantage of determining the progress of clotting.

An analysis of four cases in which there was a relatively short period of survival emphasizes the importance of complicating factors in the treatment.

CASE 1.—A Negro porter aged 29 was admitted June 24, 1934, complaining of cough, shortness of breath and pain in the upper left part of the chest. A diagnosis of sacular aneurysm of the distal transverse arch of the aorta, with perforation of the chest wall, was made. In spite of two long periods in the hospital during the ensuing year, the aneurysm grew and the symptoms became worse.

Jan. 2, 1935, 89 feet of wire was inserted into the aneurysm and heated in two stages. Symptomatic relief was immediate. Pulsation in the aneurysm diminished. Relief was maintained until the nineteenth postoperative day, when evidence of infection developed. The patient died of sepsis and secondary hemorrhage two weeks later. Necropsy showed a completely clotted sacular aneurysm with a small mouth. The position of the wire indicated absence of blood clot previous to operation.

Infection was due to accidental avulsion of the wound by the patient. The organism recovered was *Staphylococcus albus*. The wire was buried beneath the skin. In all subsequent cases the wire has been pushed entirely within the aneurysmal sac at the close of the operation.

CASE 2.—An excitable Mexican man aged 42 was admitted to Vanderbilt Clinic Sept. 30, 1932, complaining of cough and pain in the right side of the chest and a history of chancre and insufficient treatment fifteen years before. Examination revealed a fusiform aneurysm of the arch of the aorta, aortic insufficiency and high blood pressure. The Wassermann reaction was 4 plus. During four years of treatment the aneurysm became progressively larger. The heart, by electrocardiogram, showed progressive left preponderance and myocardial fibrosis. Symptoms of erosion of the chest afforded an indication for wiring. Sept. 26, 1936, operation was done in two stages. A total of 132 feet of wire was inserted into the aneurysm and heated. Relief of cough and pain was almost immediate.

December 12, three months postoperatively, there was no pain and no cough. Pulsation over the aneurysm was markedly diminished June 9, 1937, nine months postoperatively. The patient was working. There was no cough or pain. Roentgenograms showed little if any intrinsic pulsation of the aneurysm. June 27 the patient entered the hospital complaining of cough, fever and pain in the chest. A diagnosis of bronchopneumonia was made. Roentgenograms revealed no enlargement of the aneurysm since operation. However, an electrocardiogram showed an increase in the degree of damage to the heart muscle. The patient left the hospital after a few days and returned to work.

August 7 the patient was suddenly seized with an attack of precordial pain, and other symptoms were typical of coronary thrombosis. In spite of warnings he left the hospital and returned to work after two weeks. One week later he had another attack, from which he died in the hospital, several hours after admission.

By wiring, a 42 year old man having an inescapable triad of aneurysm, aortic insufficiency and hypertension was made symptom free for a period of eleven months.

CASE 3.—A Negro porter aged 50, admitted to the hospital Nov. 2, 1936, complaining of extreme shortness of breath and pain in the chest, had a history of chancre fifteen years before, treated by six injections. Ten months previous to admission he had knifelike pains in the sternal region. The Wassermann reaction was positive. He received, in all, fourteen injections of specific remedies. Three months before admission a pulsating mass appeared over the sternum and grew rapidly. Suddenly, three days before admission, the patient suffered excruciating pain and the mass became larger. Shortness of breath became extreme. On examination, the patient was

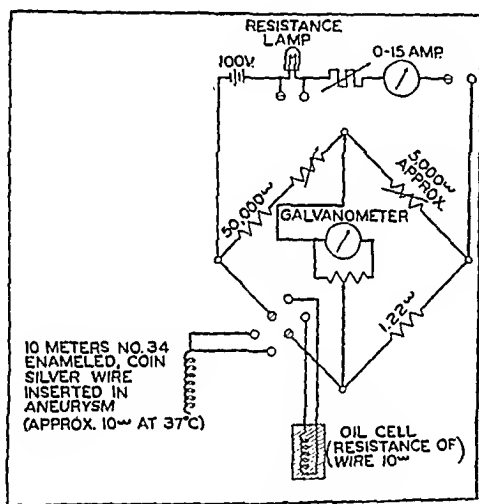


Fig. 5.—Apparatus for controlling the temperature of the wire.

to give more than a negligible impedance value. Finney,⁴ for example, reporting twenty-one cases of wired aneurysms, wisely cautioned against the use of more than from 10 to 12 feet of wire in any case.

Adherence to the sac wall of a clot deposited within an aneurysm is imperative and its organization desirable. Whereas wire alone may reinforce the blood clot, heating to 80 C. wire distributed on the inside surface of an aneurysmal sac, as advocated by us, may cause inflammation in the sac wall.

Tissue subjected to a temperature of 80 C. for a few moments reacts within twenty-four hours with edema, vascular engorgement, dilatation and a typical inflammatory reaction on the part of the white corpuscles. The peak of the inflammation is reached in from four to six days. This is followed by a period of repair, in which fibroblasts appear and tissue organization takes place with the aid of a network of budding capillaries. The entire reaction occupies from ten to twelve days, without the appearance of tissue slough.

Experimental and clinical observations have convinced us that heat inflammation is an important factor in the inactivation of aneurysms. For this reason we repeat the wiring at from ten to fourteen day intervals

4. Finney, J. M. T.: Wiring of Otherwise Inoperable Aneurysms, *Ann. Surg.* 55: 661-681, 1912.

emaciated, markedly dyspneic and cyanotic, with dilated veins in the neck and over the abdomen. A large, actively pulsating aneurysm had perforated the sternum and lay just beneath the skin. The venous and spinal fluid pressures were 140 and 300 mm. of water respectively. The Wassermann reaction of the blood was 4 plus. A roentgenogram showed a huge aneurysm of the ascending arch.

Rupture of the aneurysm seemed imminent. November 14, 132 feet of wire was inserted into the aneurysm and heated. The patient died five hours later from respiratory failure.

This case well illustrates the danger of marked pressure on the vena cava. The cyanosis, dilated veins and extremely elevated venous and spinal fluid pressures confirm this. The use of tribromethanol in amylene hydrate and gas-oxygen anesthesia was a serious error in judgment. Local anesthesia is perhaps preferable in all cases of aneurysm but imperative in cases in which there is obstruction of the vena cava.

CASE 4.—A Negro man aged 46 had been known to have an aneurysm of the thoracic aorta for twenty years. On his admission to the hospital Jan. 30, 1932, a large aneurysm of the upper part of the thoracic aorta and a small aneurysm of the ascending arch of the aorta were noted. During the next five years the patient cooperated in his treatment; as dyspnea became worse he would cut down on activity. Several periods in the hospital for a long rest were efficient in controlling the pain and dyspnea. For a few months previous to admission on Feb. 8, 1937, in spite of the medical regimen, the patient's course had been consistently downhill. Pain in the aneurysm had become continuous. A feeling of extreme tightness in the chest had increased his dyspnea. The aneurysm had become larger and extremely sensitive to pressure. It pulsated violently and lay just beneath the skin. The aneurysm of the ascending arch remained the same size during the five year period and was found subsequently to be clotted. The heart was badly compressed between the two aneurysms.

With the patient's symptoms beyond control and rupture of the huge aneurysm imminent, wiring was begun February 13. A total of 132 feet of wire was inserted and heated in two stages. The relief of pain was almost immediate. March 10, one month postoperatively, the patient had gained 10 pounds (4.5 Kg.). He had no pain and could "sleep on the protruding aneurysm." His greatest relief was a "feeling of more room in his chest to breathe." May 12, three months after operation, there was no pain and no shortness of breath with ordinary activity. The aneurysm was smaller, pulsated less and was firmer.

The patient remained essentially symptom free until December, ten months postoperatively, when there was sudden onset of pain followed by a fairly rapid growth in the size of the aneurysm. December 13, 132 feet of wire was inserted into the aneurysm and heated. No improvement resulted. December 29, 48 feet of wire was inserted and heated. Thirty-six hours later the patient died suddenly after an outcry due to pain. At necropsy the left pleural cavity was filled with blood. The huge, protruding aneurysm was partly calcified. The calcium was fractured, but the exact point of rupture of the aneurysm could not be ascertained. The wire was well distributed in the outer and inner portions of the aneurysm. Clotting had taken place up to the mouth, which was huge, making the aneurysm partly fusiform and partly saccular.

The aneurysms in these four cases were about equal in size and very large. The small amount of current required to heat the wire in case 1 was indicative of slow-moving blood within the aneurysm, which predicted a saccular aneurysm with a small mouth. Such an aneurysm was found at necropsy. At operation a thorough needling of the aneurysm failed to return blood. This was considered indicative of complete clotting, which was verified at necropsy.

In case 1 only 89 feet of wire was required to cause mass clotting, whereas in case 3 132 feet of wire was required. Because of this and the higher amperage

necessary to heat the wire, it was believed that, even though the aneurysms were of comparable size, the aneurysm in case 3 had a much larger mouth. In case 3, for example, it required 5 amperes to heat to 73 C. each of the first two 33 foot segments. The third segment required 4 amperes. The fourth 33 foot segment had so slowed the blood as to require only 3 amperes to heat, and, as expected, complete mass clotting took place.

The aneurysm in case 2 was considered fusiform, and it is of interest that the current requirement, 6.7 amperes, to heat the first 33 foot segment of wire was considerably higher than in cases 1 and 3, as might be expected for a very rapid blood flow. However, the fourth 33 foot segment of wire inserted slowed the flow to such an extent that it required only 4 amperes for heating. Sufficient mass clotting took place in this case to arrest the pulsation and inactivate the aneurysm.

Another type of aneurysm, that in case 4, received the same amount of wire, namely 132 feet, as did the aneurysm in cases 2 and 3, but after ten months began to grow. The blood velocity in this aneurysm was so great that even after the insertion of 132 feet of wire it required 6.3 amperes to heat the last 33 foot segment to only 61 C. We know now that complete mass clotting never takes place when blood moves rapidly; this was proved when exploration of the aneurysm ten months later revealed a large unclotted cavity. That the velocity of the blood was effectively reduced and clotting obtained by the subsequent addition of 180 feet of wire was shown at necropsy. These results suggest that if the entire 310 feet of wire had been inserted at the first operation the aneurysm might have remained inactive. Just what part, if any, fracture of the calcified wall played in the subsequent rupture is a matter of conjecture.

CASE 5.—A Negress aged 51, who entered the Vanderbilt Clinic March 30, 1931, eight years previously had received forty injections for syphilis. Her complaint was pain along the right side of the sternum and cough of several weeks' duration. Examination revealed a moderately active pulsating aneurysm of the ascending arch and a stricture of the rectum. The Wassermann reaction of the spinal fluid was positive. The patient was treated consistently from 1931 to 1935, during which time the aneurysm gradually grew. Because of beginning erosion of the chest, the development of throbbing pain, dyspnea and cough, and recurrent attacks of bronchitis, wiring became advisable. March 16, 1935, 53 feet of wire was inserted into the aneurysm and heated. A thorough exploration of the aneurysm with a needle at the close of the operation revealed it to be clotted. Relief of pain was complete after operation. May 4, two months postoperatively, there was no pain and no cough and the dyspnea was less. No pulsation was seen over the aneurysm. Feb. 15, 1936, eleven months postoperatively, there was no pain, no cough and no shortness of breath with normal activity. The aneurysm was needled and no free blood encountered. Twenty cc. of skiodan was injected into the aneurysm and remained there for days. Roentgenograms revealed the aneurysm to be smaller than before operation. April 8, 1938, three years postoperatively, the patient was symptom free and no pulsation was seen or felt. In August 1938, three years and five months postoperatively, she was symptom free and no change was seen in the aneurysm.

CASE 6.—A Negress aged 32, admitted to the hospital June 4, 1935, for two months had suffered from a throbbing pain to the right of the sternum and pain in the right scapular region. She suffered from cough, shortness of breath and night sweats. Fluoroscopic examination revealed a pulsating, fusiform aneurysm of the ascending arch. The heart was slightly enlarged; the Wassermann reaction was 4 plus. Moderately severe anemia was present.

Wiring of the aneurysm was begun September 17; 198 feet of wire was inserted and heated in three stages. Relief of pain and cough was prompt. Pulsation over the aneurysm became scarcely discernible. Shortness of breath improved, but anemia persisted. Sept. 30, 1936, one year postoperatively, the patient was operated on for a pelvic abscess. Her anemia and shortness of breath disappeared after convalescence from the pelvic peritonitis. Sept. 17, 1937, two years after wiring, no intrinsic pulsation could be demonstrated in the aneurysm either fluoroscopically or by roentgenkymogram. May 24, 1938, two years and eight months postoperatively, the aneurysm was inactive and the patient symptom free. In August 1938, two years and eleven months postoperatively, she was symptom free and leading a normal life.

This fusiform aneurysm, half the size of the saccular aneurysm in case 1, required double the amount of wire. Fortunately our method of heating affects only the wire within the sac. Wire crossing the fast, axial current of a fusiform aneurysm because of cooling remains uncoated by protein coagulum. To heat the first 10 meter segment of wire in case 6 to 73 C. required 7.5 amperes, whereas additional wire had so slowed the blood that only three amperes was necessary to heat the last 10 meter segment to 83 C. At the close of the operation concentric clotting had taken place to the extent of narrowing the channel available to blood flow to three-fourths inch.

CASE 7.—A West Indian laborer aged 37, admitted to Vanderbilt Clinic March 4, 1936, for two years had suffered pain in his back, mild at first but getting progressively worse. A roentgenogram revealed an aneurysm of the abdominal aorta, with marked erosion of the eleventh and twelfth dorsal and the first lumbar vertebrae. The Wassermann reaction was positive. During five months of antisyphilitic therapy the pain continued in the back in the region of the aneurysm. It became radicular and was only partly relieved by opiates. The patient was rapidly becoming bedridden; the muscles of the back were "frozen." Loss of weight and weakness progressed. Laparotomy Aug. 10, 1936, revealed a medium-sized saccular aneurysm arising from the posterior wall of the abdominal aorta, as indicated by roentgenogram. The special needle was inserted through the anterior wall of the aorta opposite the sac of the aneurysm and 33 feet of wire was introduced. Most of the wire accumulated in the mouth of the sac, which was unusually small. The patient's statement of immediate relief of pain was confirmed when he began to get around. The spasm in the muscles of the back began to disappear. Six weeks after operation the aneurysm was thoroughly explored with a 14 gage needle and found to be completely clotted. Feb. 6, 1937, six months postoperatively, the patient was back at work without a complaint and gaining weight. The back, of the ramrod type before operation, now has 100 per cent function in all directions. May 12, 1937, nine months postoperatively, roentgenograms revealed no further destruction of bone. The patient has gained 26 pounds (12 Kg.) since operation. August 25, twelve months postoperatively, a roentgenkymogram revealed no pulsation of the aneurysm. The patient worked regularly without symptoms. April 8, 1938, one year and eight months postoperatively, he was symptom free; there was no evidence of activity in the aneurysm. He was carrying on his job as truck driver's helper. In August, two years postoperatively, he was symptom free. There was no further erosion of the vertebrae. He continued his work loading trucks.

CASE 8.—A Negress aged 32, admitted to the hospital Oct. 7, 1935, for six months had been having pain in the upper left part of the chest, front and back. She suffered from dyspnea, cough and, more recently, hemoptysis and night sweats. Examination revealed a saccular aneurysm arising from the posterior wall at the distal one third of the transverse arch. The Wassermann reaction was positive. During the ensuing year rest and antisyphilitic therapy seemed to control most of the patient's symptoms. The aneurysm grew, however, and suddenly, in October 1936, the patient had a massive pulmonary hemorrhage, for which she was hospitalized. Within a month

a second massive hemorrhage rendered her unconscious. From this time until her operation, Jan. 15, 1937, her course was rapidly downhill. There was pain requiring codeine for relief. Considerable hemoptysis occurred frequently during the day; dyspnea was distressing. The patient entered the hospital with cough and fever and in agonizing expectancy of a final gush of blood from her mouth. She was given transfusion, and a total of 165 feet of wire was inserted into the aneurysm and heated in two stages. A moderate pulmonary hemorrhage occurred after a coughing spell during the first operation. After wiring the pain quickly disappeared. Within three months she had gained 11 pounds (5 Kg.) and returned to work. Fourteen months postoperatively she informed us by letter that she continued to work, had gained 14 pounds (6.4 Kg.) and had no hemoptysis, cough or dyspnea. Rarely she has "slight pain in the aneurysm." In August, one and one-half years postoperatively, she had no pain, no shortness of breath, no cough and no hemoptysis; there was no change in the aneurysm, and she carried on her job operating a beauty parlor.

CASE 9.—A Negress aged 28 entered Vanderbilt Clinic March 23, 1936, complaining of difficulty in breathing of one and one-half years' duration, with cough, difficulty in swallowing and attacks of choking at night of five months' duration. She had been receiving antisyphilitic therapy elsewhere. Examination revealed a rather small aneurysm arising from the anterior wall of the distal third of the transverse arch. The aneurysm had paralyzed the left recurrent laryngeal nerve and compressed the left bronchus. During the next ten months pain developed along the left sternal border. The patient was admitted to the hospital May 2, 1937, with a bad cough, fever and marked stridor. Roentgenograms revealed almost complete occlusion of the left bronchus. May 15, wiring of the aneurysm was begun; 139 feet of wire was inserted and heated in two stages. One month after operation the patient was free from cough, there was no pain along the left sternal border and the dyspnea had vastly improved. A roentgenkymogram revealed a diminution in pulsation of the aneurysm. Three months after operation the patient went through a long siege of pelvic peritonitis, with fever and menorrhagia. Dizzy spells were an annoying feature of this illness. May 15, 1938, one year postoperatively, the patient was totally free from her original pain and was the picture of health. She was free from cough and dyspnea except when she had a cold or climbed stairs. There was still some wheezing, however, when she walked fast. In August, one year and three months postoperatively, her condition was unchanged.

CASE 10.—A Latvian laborer aged 68, admitted to the hospital Nov. 27, 1938, complaining of cramplike and throbbing pain in midabdomen, loss of weight and weakness of two months' duration, had a large pulsating aneurysm of the abdominal aorta, causing marked pressure on the duodenum. There was 30 per cent gastric retention. The Wassermann reaction was 4 plus.

At the end of a year's treatment the patient had, in addition to the crampy pain, a dull and throbbing pain over the aneurysm and lumbar pain so severe as to require codeine for relief. Duodenal obstruction became so marked that the patient, to avoid vomiting, took only fluids.

Dec. 30, 1937, 91 feet of wire was inserted into the aneurysm and heated. Ten days after operation the patient was eating a regular diet without a digestive symptom, and was totally free from pain. March 23, 1938, three months postoperatively, the patient had gained strength and 11 pounds (5 Kg.) in weight. He ate any food and was symptom free. The aneurysm seemed smaller and firmer and pulsated less. In August 1938, eight months postoperatively, he was symptom free and the aneurysm was unchanged.

CASE 11.—A Negro laborer aged 41 was admitted to the nose and throat department Nov. 17, 1937, moribund from tracheal obstruction. Examination revealed cyanosis, great respiratory stridor and pulmonary edema. A saccular aneurysm arising from the posterior wall of the aorta at the junction of the ascending and transverse arch caused almost complete occlusion of the trachea at the level of its bifurcation. Helium and oxygen, under pressure, relieved the patient's respiratory distress considerably. December 30, 109 feet of wire was

inserted into the aneurysm and heated. Three weeks later an additional 48 feet was inserted. Two weeks after operation the patient could assume any position without respiratory distress. March 8, 1938, three months postoperatively, he had gained 12 pounds (5.4 Kg.) and could walk slowly without dyspnea. April 27, four months postoperatively, he walked twenty-nine blocks and climbed stairs without shortness of breath. He was symptom free. A roentgenkymogram showed marked reduction of pulsation in the aneurysm. In August, eight months postoperatively, he was symptom free and had been working at his job as a truck driver for the past four months.

In spite of the fact that this man had mild hypertension, there was no evidence of aortic insufficiency and inactivation of his aneurysm may add years to his life.

In six of the seven living patients relief of symptoms has been complete. Patient 9, with almost complete occlusion of the left bronchus before operation, had slight dyspnea on climbing stairs one year and three months after operation.

The longest follow-up is three years and five months (case 5) and the shortest eight months. One fusiform aneurysm, in case 6, has been inactive for two years and eleven months. There are two patients with abdominal aneurysms: patient 7, with marked vertebral erosion, symptom free for two years, and patient 10, well eight months postoperatively. There are three aneurysms of the transverse arch with marked tracheo-bronchial pressure, in cases 10, 9 and 7.

Demonstration by roentgenograms of small changes in the size of the aneurysm after wiring is difficult. It seemed definite in case 5 (fig. 3). However, a reduction in size in case 7 made the difference between agonizing radicular pain and comfort. In case 8 it eliminated bronchial erosion and hemorrhage. In case 9 it averted death by strangulation.

Roentgenkymography has been of great help in showing the effect of induced clotting on the pulsation of aneurysm (fig. 4).

Whereas it is fair to assume in retrospect that rupture of the aneurysm in case 4 might have been avoided, the patient lived symptom free for more than ten months.

H. A. Christian,⁵ in a review of forty cases of wired aneurysms, reported that ten of the patients (25 per cent) died of rupture within seven months after operation, eight of the ten dying within the first two months.

Sir D'Arcy Power⁶ reported twenty-one cases, in seven of which (33 per cent) death from rupture occurred within two months after wiring.

CONCLUSION

We believe that a thoroughly clotted aneurysm may be inactivated indefinitely. Our method of clotting saccular and fusiform aneurysms, if used according to the technic described, is safe and efficient. Heating the wire to 80 C. causes a heat inflammation within the sac wall, which promotes adherence and organization of the clot deposited. We conclude that the absence of signs or symptoms of growth of the aneurysm in seven living patients operated on by this method and the relief of pain and symptoms due to distressing pressure justify us in recommending the procedure.

One Hundred and Sixty-Eighth Street and Broadway-

5. Christian, H. A.: Aneurysms of the Thoracic Aorta Treated by Wiring. Boston M. & S. J. 166: 122-127 (Jan.) 1912.

6. Power, Sir D'Arcy: The Palliative Treatment of Aneurysms by "Wiring" with Colt's Apparatus. Brit. J. Surg. 9: 27-36 (July) 1921.

BRONCHIAL ASTHMA

ITS DIAGNOSIS AND TREATMENT

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Through the evolution of the knowledge of allergy, especially in the last two decades, complete relief is often available for most patients suffering with bronchial asthma. At first the recognition of the role that inhalant allergy exerts in the disease was of great help. Then in the last decade the frequency of food allergy as a major and often a complicating cause and the relegation of bacterial allergy to its usual minor role have contributed most to improve our possible results.

An analysis of the results of the treatment of 1,443 private patients seen during the last fifteen years who have cooperated with at least fair satisfaction for six or more months is shown in table 1. Excellent or good results were obtained in approximately 80 per cent and fair results in 13 per cent. Poor results occurred in 7 per cent. Death occurred during attacks in six patients with long standing bronchial asthma. No morphine had been used except by one patient, who had taken it without order for some years. Death has also occurred, attributed largely to morphine, in two other cases, seen

TABLE 1.—Results with 1,443 Private Patients with Bronchial Asthma Who Have Given Fair Cooperation for at Least Six Months

Results	0-15 Yrs. (469 Cases) Per Cent	16-55 Yrs. (783 Cases) Per Cent	55 and Up (191 Cases) Per Cent	1,443 Cases Per Cent
Poor.....	4	9	8	7
Fair.....	10	13	10	13
Good.....	27	26	33	27
Excellent.....	59	52	49	50

only in consultation. Such fatalities from chronic asthma emphasize continued study and treatment until satisfactory results are assured. In table 2 it is seen that favorable results are not greatly influenced by the duration of the disease. It is obvious that, if the cooperation had been better, these statistics would have been more satisfactory.

The procedures of diagnosis and treatment developed by many students of allergy since 1912 which I¹ have utilized will now be discussed.

A carefully recorded history taken with the possibility of all types of food, drug, inhalant, bacterial and parasitic allergy in mind is of the greatest importance. Rackemann² stated that the history is often of more importance than skin testing in diagnosis. Correlation of the symptoms with foods, medicines, seasons and environments is imperative. Thus asthma that is better in the summer and worse in the fall, winter and spring should suggest food allergy and, to a less extent, animal emanation, dust and other inhalant allergies encountered during these months. The history of recurrent asthma starting at the age of from 18 to 20 months, preceded frequently by infantile eczema, again points to

Read before the Section on Practice of Medicine at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 16, 1938.

1. Rowe, A. H.: Clinical Allergy: Manifestations, Diagnosis, and Treatment, Philadelphia, Lea & Febiger, 1937.

2. Rackemann, F. M.: History Taking in Allergic Diseases, J. A. M. A. 106: 976 (March 21) 1936.

possible food sensitization. Increased asthma on week ends or on Mondays suggests overindulgence in foods or added inhalation of dusts or other allergens from home or social sources. Bacterial allergy must not be blamed merely because of true or apparent "colds," pneumonia or whooping cough before the original or recurrent attacks. Usually such "colds" are evidences of localized allergy rather than infection, the ensuing asthma resulting from an extension of such allergy to the lungs.

The systematic recording of the history expedites the diagnosis and may be recorded under the following headings:

- 1. Bronchial manifestations: Onset, frequency, periodicity and chronicity of the attacks or persistent symptoms, the amount and character of sputum, frequency and degree of cough, fever, complications and former history of bronchial symptoms.
- 2. Nasal and sinal symptoms: Duration, amount and degree of seasonal or perennial nasal congestion, blocking, sneezing, itching, nasal or postnasal discharge, sinal congestion or pain, and former history of head colds or sinusitis.

TABLE 2.—Influence of Duration of Bronchial Asthma on the Results of Treatment in 873 Cases

Years of Bronchial Asthma	Degree of Relief	Number of Patients	Per Cent of Patients
0 to 2	Poor.....	32	11
	Fair.....	54	19
	Good.....	61	22
	Excellent.....	133	48
3 to 7	Poor.....	20	7
	Fair.....	49	17
	Good.....	87	30
	Excellent.....	137	46
8 or more	Poor.....	27	8
	Fair.....	28	17
	Good.....	39	23
	Excellent.....	63	50

- 3. Dermatoses: Onset, duration and distribution of allergic dermatitis (eczema), contact dermatitis, urticaria or angioneurotic edema during life, with possible etiologic comment.
- 4. Gastrointestinal symptoms: Occurrence of canker sores and other oral, gastrointestinal and abdominal symptoms with their duration, degree, characteristics and possible relation to allergy.
- 5. Recurrent headaches, migraine, biliousness, fatigue or "toxic states."
- 6. Genito-urinary, cardiovascular, glandular, nervous or psychoneurotic disturbances, with data for or against allergy as a primary or complicating cause.
- 7. Dietary history: Dislikes or disagreements for foods of all types, and habits of eating. Questions such as Do you drink milk, eat eggs or spinach? may suggest allergy, digestive inefficiency, whims, fancies or psychoneuroses as causes. Potential or active nutritional deficiencies must be recognized, as emphasized by Minot.
- 8. Drug history: Possible allergy to medicaments used even infrequently.
- 9. Environmental history: The kind of carpet, curtain, furnishings, mattress, pillow, bedding, fur, clothing, animal, plant, flower, cosmetic, toilet accessories and other similar information concerning the living, sleeping, working and recreational environments; likewise the names of trees, shrubs and flowers, the character of the surrounding region, whether built up or in the country, its proximity to barns, animals, fields, orchards, forests or marshes, the amount and character of dusts and similar information.

- 10. Family history: Bronchial, nasal, cutaneous, gastrointestinal or other symptoms, especially migraine, recurrent headache, toxic or bilious states in several generations and progeny, with a record of possible familial ingestant inhalant or contact sensitizations. Other usual information concerning familial diseases, longevity and dietary habits.
- 11. Residences: Their possible relation to allergy.
- 12. Past history: Past or present infections or illnesses not already noted.
- 13. Menstrual history and the possible influence of allergy.
- 14. Operations: Year and results of operations, especially on the nose and throat.
- 15. Habits: Amount of tobacco and alcohol and their influence on allergy.

DIFFERENTIAL DIAGNOSIS

In the study of all symptoms of possible allergic origin it is most important to conduct a thorough physical examination and indicated laboratory studies to determine other possible causes. In possible bronchial asthma, one must have the various causes of dyspnea in mind.³ Some of the important ones are pharyngeal abscess or tumor, laryngeal spasm (especially croup), laryngeal inflammation (acute and chronic), edema and stenosis, foreign bodies and neoplasms and paralysis of the vocal cords; tracheal and especially bronchial infection or inflammation (at times with stenosis), pulmonary atelectasis or pneumothorax, emphysema, neoplasm and at times bronchioliths or stones; external pressure from thyroid enlargements or carcinoma, thymus enlargements, aneurysm, enlarged or infected tracheobronchial nodes and mediastinal growths; pneumonia, tuberculosis of the lungs, pneumoconiosis, pulmonary fibrosis, cystic diseases of the lungs, pneumothorax and hydrothorax; cardiac decompensation, coronary sclerosis, auricular flutter or fibrillation, paroxysmal tachycardia, Ayerza's disease, coarctation of the aorta, renal sufficiency, acidosis, alkalosis or oxygen lack; functional and hysterical dyspnea, lesions of the respiratory center, and disturbances in the muscular function of the thorax and diaphragm.

When severe attacks of bronchial asthma or long standing recurrent symptoms with the typical hyperresonance, prolonged expiration with musical sibilant or coarse rales and rhonchi and varying degrees of wheezing are present, the diagnosis is quite assured; but when bronchitis is recurrent, associated with some wheezing and varying types of rales, inhalant or ingestant allergy may receive unwise emphasis. This occurred in one patient aged 65 whose symptoms were later relieved elsewhere by extraction of infected teeth and clearing of infection in the sinuses. Cystic disease of the lungs, pulmonary fibrosis, atelectasis, foreign bodies and emphysema have also caused symptoms suggesting bronchial asthma. However, the finding of obvious pathologic conditions which might explain asthmatic symptoms must not divert attention from possible ingestant or inhalant causes. Thus, in a boy aged 12 years who had had recurrent bronchial asthma for several years, remarkable diffuse calcified areas throughout both lungs were revealed by x-ray examination but his symptoms were entirely relieved by elimination diets. Also a woman aged 60 with elimination diets was relieved of long standing asthma, formerly attributed to marked pulmonary fibrosis.

X-ray studies may also reveal important pathologic changes in the thorax or lungs. With nasal symptoms a rhinologic examination is advisable. Opacity, cloud-

3. Maytum, C. K.: Differential Diagnosis of Asthma, M. Clin. North America 14:729 (Nov.) 1930.

ing or mucosal thickening in the sinuses occurs more often from allergy than from infection.

The fact that long standing chronic asthma often leads to increasing emphysema and chronic bronchitis, and at times may result in bronchiectasis, in occasional atelectasis or in massive collapse of the lung (spontaneous pneumothorax), and not infrequently leads to death, stresses the importance of adequate study and control of all allergenic causes. The deformities of the chest, the retardation in growth and impaired nutrition which arise from uncontrolled asthma in childhood refute the assertion that the "child will outgrow his asthma."

TESTING FOR ALLERGY

All patients with possible bronchial asthma or allergic bronchitis should be tested with all food, animal emanation, dust, fungus and miscellaneous allergens, together with all tree, spring, summer, fall and cultivated flower pollens that might be ingested or inhaled. The results of the routine testing of 1,700 private patients are given in table 3. Testing must be done by one experienced in the technic of testing. Active allergens known to produce positive reactions in clinically sensitive patients must be used. Unquestioning dependence on such cutaneous tests rarely leads to good results, since cutaneous reactions are often negative to food and less often to inhalant allergens productive of clinical allergy. Moreover, nonspecific or irritant reactions occur, especially from intradermal testing with food allergens. Positive cutaneous reactions also may indicate only potential allergy. Therefore, positive cutaneous reactions are only guides to diagnosis, and their clinical importance must be checked by history, ingestion or inhalation.

As a routine, scratch testing should first be done with all allergens already noted. Thereafter, intradermal testing is advisable with 1:200 dilutions of all inhalant allergens of importance from the patient's point of view and to which negative scratch reactions have occurred. I have not used intradermal testing with food allergens as a routine for reasons previously stated.⁴ Elimination diets are usually utilized for the additional study of possible food allergy. Because of varying skin reactivity, retesting at times in poorly controlled cases is necessary. With this plan of testing, the routine study can be completed in from one to three days, depending on the time that can be allotted by the physician. Such complete and rapid testing in infants and young children, however, must be varied according to the problem presented. For the details of technics, the type of allergens, syringes and needles used and the interpretation of the reactions, standard textbooks must be consulted.⁵

Because of the indefinite or negative cutaneous reactions that may arise, auxiliary methods for diagnosis have been developed.

1. Trial diets are of greatest importance in the diagnosis of food allergy. For this I continue to use my elimination diets¹ when I suspect food allergy which is not controlled with test-negative diets. In fact, when cutaneous tests are impossible the initial use of elimination diets is justifiable. Only with a trial diet used for several weeks or even months can food allergy be ade-

quately studied. Trial diets will be used without results on many patients, but not as frequently as are other laboratory procedures. However, and this must be emphasized, if any nutritional deficiency or undesirable loss of weight arises from insufficient vitamin, protein or calory intake, such trial diets should be discontinued. Uncontrolled food allergy is preferable to the serious results of inadequate nutrition.

Though the choice and use of the elimination diets cannot be fully discussed, a few comments will be offered. Trial diets may be started with diets 1 and 2 combined, for which menus have been published.¹ If a history of probable idiosyncrasies to specific foods or groups of foods such as citrus fruits, the pit fruits or the legumes is obtained, or if definite scratch reactions

TABLE 3.—Results of Routine Cutaneous Testing in 1,700 Cases of Bronchial Asthma*

	536 Cases: 0-5 (177) 6-10 (236) 11-15 (123) Per Cent	949 Cases: 16-35 (431) 36-55 (408) Per Cent	215 Cases: 55 Yrs. Up Per Cent	Total 1,700 Cases Per Cent
Positive family history....	67	50	34	60
Males.....	63	46	44	53
Females.....	23	54	56	47
Pollen sensitization:				
1+ reactions.....	27	18	18	22
2+ or 3+ reactions.....	27	41	23	30
Food sensitization:				
1+ reactions.....	30	20	20	23
2+ or 3+ reactions.....	18	15	13	17
Animal emanation sensitization:				
1+ reactions.....	32	23	20	24
2+ or 3+ reactions.....	18	23	17	20
House dust sensitization:				
1+ reactions.....	26	24	25	25
2+ or 3+ reactions.....	20	27	11	19
Orris sensitization:				
1+ reactions.....	4.0	6	3	5
2+ or 3+ reactions.....	1.1	3	2	2
Miscellaneous sensitizations:				
1+ reactions.....	10	10	3	8
2+ or 3+ reactions.....	4	8	2	6

* Scratch tests with food allergens; intradermal tests only with inhalant allergens which failed to react by the scratch method.

have occurred to specific foods, they should be excluded, it being remembered, however, that only actual ingestion of such foods when the patient is symptom free can prove their allergenic activity. If positive cutaneous reactions or probable clinical symptoms are present to wheat or other cereals, trial diets may be started with cereal-free diet 3. In the use of the elimination diets, absolute cooperation is imperative.⁶ Bread and bakery products must be made with ingredients of unquestioned purity, according to published recipes. Honest bakers must work under the direct supervision of the allergist. Foods eaten in restaurants, friends' homes and hotels must be free of every trace of ingredients not included in the diet. A taste or trace of a food may confuse the interpretation of results. The cooking of foods must be most particular. Food should not be stirred with a spoon that has touched milk or any other

4. Rowe, A. H.: The Evaluation of Skin Reactions in Food Sensitive Patients, *J. Allergy* 5: 135 (Jan.) 1934.
5. Tuft, L.: Clinical Allergy, Philadelphia, W. B. Saunders Company, 1937.
6. Bray, G. W.: Recent Advances in Allergy, Philadelphia, P. Blakiston's Son & Co., 1937.
Vaughan, W. T.: New book, to be published.
Hansel, F. K.: Allergy of the Nose and Paranasal Sinuses, St. Louis, C. V. Mosby Company, 1936. Rowe.¹

6. Rowe, A. H.: The Dietary Problem of the Food Sensitive Patient, *Am. J. Digest. Dis. & Nutrition* 4: 757 (Feb.) 1938.

forbidden food before it has been washed. Similar care of cooking utensils, knives and dishes must be observed.

If relief is not evidenced in two or three weeks, another elimination diet should be tried, provided proper weight and nutrition are maintained. Finally, if food allergy is likely and the routine diets have failed, the use of my supplemental diets¹ which exclude groups of foods such as vegetables, fruits, meats or cereals may be used, but never if nutritional damage is likely. If milk is excluded for more than two weeks, especially in infancy, extra calcium should be ordered. When sunshine or quartz light is not available, viosterol in an oil included in the diet should be prescribed. The exclusion of important foods such as milk, egg or wheat should never continue for more than a few weeks unless clinical testing with such foods demonstrates resultant symptoms from them. Above all else, the patient must be interviewed every few days to determine any dietary mistakes and to prescribe indicated additions or changes.

2. For the study of food allergy, the leukopenic index as described by Vaughan² and recommended by Rinkel, Gay, Squires and others has been advised. In my practice, since this test is time consuming and subject to technical error, and because of the necessity of using trial diets to confirm the clinical significance of a positive index, it has been used only in a few selected cases.

3. Diet diaries may yield important information, though the careful questioning about possible mistakes in dieting or concerning reactions from foods usually makes such diaries unnecessary.

4. Negative cutaneous reactions to pollens and other inhalants productive of clinical allergy may occur, possibly in from 10 to 20 per cent of such sensitizations. Lack of skin-sensitizing bodies is responsible, though such bodies are usually present in the mucous membranes of the eyes, nose or bronchi. Hence the ocular, nasal or intrabronchial tests with the dry allergens or their extracts are used to obtain more specific information about inhalant allergens suspected through history. The technic of such tests is described in current textbooks.

5. The passive transfer, or Prausnitz-Küstner reaction, at times will reveal positive cutaneous reactions not obtainable in the patient. Cowie³ reports increased skin reactivity in the actual patient when the tested areas have been injected twenty-four hours previously with autogenous serum. The practical value of these tests is restricted and usually must be utilized by specialists in selected cases.

6. Environmental control that eliminates practically all air-borne allergens is of value in the study and treatment of suspected inhalant allergies. When house dust, animal emanation and other miscellaneous sensitizations are present, the covering of pillows and the mattress with dust-proof covers, the use of washable cotton blankets, the removal of overstuffed furniture, the use of washable curtains and rugs and the thorough wiping of ceilings, walls, floors and all furniture and other surfaces so that all dust is eradicated will often yield desired information. If pollens and other outdoor inhalants are suspected, a pollen filter which throws inhalant-free air into the room is frequently necessary. If money is available, an air conditioning unit which not only filters but controls the temperature of the air

is desirable. Relief occurring in a few days favors inhalant allergy. Such an environment may be necessary until specific desensitization offers adequate protection.

7. The final diagnosis of the allergenic causes of bronchial asthma must depend on the results of treatment. Thereby it is gradually determined what foods or other ingestants cause the symptoms and what inhalants must be avoided or must be included in anti-gens for hyposensitization therapy. Likewise, the less frequent role of bacterial allergy can be determined only after the results of vaccine therapy and removal of foci have been noted. At times the many specific causes of bronchial asthma remain in doubt for months and, as good or excellent relief occurs, such etiology may never be incontrovertably proved.

TREATMENT

Treatment is best considered under the following headings:

1. Inhalant sensitizations to certain pollens, animal or insect emanations, dusts and miscellaneous allergens at times may be controlled by their elimination from the patient's environment. Usually, however, hyposensitization with etiologic allergens is necessary. Specific therapy with individual grasses, feathers or other allergens is usually required. Moreover, the autogenous house or other dust extract is to be chosen in place of stock preparations. The initial dose of an antigen should be 0.05 or 0.1 cc. of a dilution which fails to react by the scratch method. Such a dilution is usually a 1:5,000 or a 1:50,000 dilution, though at times, as in some allergies to silk or glue, the dilution for the initial treatment may have to be as dilute as one to five or even to five hundred million. The method of increasing the doses, the maximum amounts indicated, the duration of therapy and other considerations concerning hyposensitization treatment must be obtained from current publications.^{4a} In general, treatment must not increase or reestablish allergic symptoms, especially during pollen seasons, when coseasonal therapy with small doses of a 1:50,000 or 1:5,000 dilution given every one or possibly two days is usually very beneficial. In the absence of definite symptoms, maximum doses of from 0.5 to 1.0 cc. of a 1:50 dilution can gradually be reached and repeated every one to two weeks for perennial therapy. The duration of such treatment must vary with the patient's allergy and the persistence of the established hyposensitization. The prompt control of general reactions with from 0.3 to 0.8 cc. of a 1:1,000 solution of epinephrine hypodermically must be stressed. This dose should be repeated every five to thirty minutes until symptoms are well controlled. A tourniquet placed above the site of injection, loosened every five minutes for one minute over a period of twenty or thirty minutes, retards antigen absorption.

When sensitization is present to animal emanations, dusts and other inhalants in the living or working environment, elimination of such inhalants is often necessary. Such environmental control, at least until hyposensitization has been achieved, is necessary. During the pollen season, pollen filters or air conditioners may also be necessary until protection is afforded by proper therapy. In the patient sensitive to house dust the amount of necessary environmental control varies with the patient's susceptibility and the results of house dust therapy.

7. Vaughan, W. T.: Leukopenic Index as a Diagnostic Method in the Study of Food Allergy, *J. Lab. & Clin. Med.* 21:1278 (Sept.) 1936.

8. Cowie, D. M.: Autopassive Transfer in Allergy, *Ann. Int. Med.* 11:949 (Dec.) 1937.

8a. Rowe,¹ Tuft,⁵ Vaughan.⁵

With uncontrolled patients, attention must be directed to possible fungus allergy,⁹ which seems more frequent than has been appreciated, and also to the action of unusual or unsuspected inhalant allergens, the discovery of which may require a special study of the home or outdoor environment.

2. Food sensitizations are best controlled by the continued elimination of the causative foods. Increased tolerance may arise in a few weeks, but usually months and at times years are necessary. The use of denaturized foods such as evaporated milk may be effective in certain mildly sensitive patients but fails when marked allergy is present. The possibility of increasing tolerance by the hypodermic administration of food allergens or by the gradual feeding of such foods must be kept in mind, though in the hands of most allergists this has not been especially successful. As already stressed, the longer continued elimination of foods is justified only when a diet containing proper proteins, vitamins, minerals and calories is possible which meets all nutritional requirements and maintains a satisfactory weight.

Other ingestants such as drugs, minerals including chlorine and calcium, and organic or other substances in water to which allergy occasionally arises must be excluded for relief.

3. My opinion coincides with that of most allergists that bacterial allergy is much less frequent, especially as a major cause of bronchial asthma, than seemed likely two decades ago. Thus, an exhaustive study of the possibilities of inhalant and ingestant allergies must be made before much stress is placed on bacterial sensitizations. However, in cases resistant to such effort, bacterial allergy should be studied. Foci of infection, especially in the gums, around the teeth and in the sinuses, rectum and even gallbladder and appendix must be suspected. Surgery alone, however, on the nose and throat rarely benefits patients with asthma¹⁰ and is indicated only to remove definite nasal infection or obstructions when underlying allergies are under control.

Autogenous vaccines may be prepared not only from such foci but also from the sputum. Harley¹¹ recently confirmed the skepticism of others as to the value of immediate or delayed cutaneous tests as indicators of causative bacterial allergens. He advised the initiation of vaccine therapy with doses of not more than one million subcutaneously, the dose being gradually and cautiously increased every five to seven days according to the relief obtained. Continued administration of such vaccine every one to three weeks for a year or more may be advisable. A stock respiratory vaccine may be as effective as an autogenous one. In a few cases I have used such vaccine by vein in a suspension of one million to the cubic centimeter. Of this, from 0.05 to 0.1 cc. has been given every four to seven days with a gradual slight increase according to the results, with excellent benefit in a few isolated cases. Whether the effect is due to specific or to nonspecific action is difficult to determine.

4. As for general therapy, (a) The hypodermic administration of a 1:1,000 solution of epinephrine continues to offer the best relief to bronchial asthma. In doses of from 3 to 12 minims (0.2 to 0.8 cc.) according

to the age and severity of the symptoms, such treatment can be repeated every five to thirty minutes as necessary for relief. Its effect is enhanced at times if given slowly. Intravascular injection must be prevented. In recurrent asthma, self administration is justified.

The inhalation of a 1:100 solution of epinephrine¹² has decreased the necessity of the subcutaneous injection of a 1:1,000 dilution for the relief of moderate symptoms. Potent preparations in vaporizers throwing off a good volume of vapor must be assured.

(b) Ephedrine sulfate in doses of from three-eighths to three-fourths grain (0.02 to 0.05 Gm.) by mouth relieves some patients. The nervousness resulting from this drug is reduced by its combination with various barbiturates. In combination with a theobromine and a barbiturate the effectiveness at times is increased.

(c) Iodides maintain their long recognized value in bronchial asthma. The saturated solution of potassium or sodium iodide in doses of from 5 to 20 drops two to four times a day according to the age and the type of asthma is generally used. Its combination with tincture of stramonium or lobelia or with ipecac or apomorphine enhances the relief in some cases. With its use the occurrence of marked nasal congestion, headache, swelling of the salivary glands and acneform lesions of the skin may contraindicate its continuance.

(d) Morphine is contraindicated for the relief of bronchial asthma. Repeated epinephrine therapy will control practically all attacks until the treatment based on specific inhalant or ingestant causes produces results. In severe intractable asthma, morphine even in small doses may decrease voluntary breathing, leading to asphyxia and not infrequently to death.

(e) The decrease and expulsion of bronchial mucus is of great importance for the relief of bronchial asthma. For this, iodide and at times ipecac therapy are most helpful. In intractable asthma which does not yield to the control of possible ingestant, inhalant or bacterial sensitizations, mild etherization, usually by rectum,¹³ may produce bronchial relaxation, with subsequent mucoid expectoration. When adherent mucus, bronchial casts or other bronchial obstructions are suspected as causes of resistant asthma, bronchoscopy may be of value.

Recently the intrabronchial instillation of iodized oil¹⁴ has been advised in most cases of resistant asthma. When retained mucus may be exaggerating the symptoms, such oil may be required, though, with proper treatment directed against existing allergenic causes, the asthmatic symptoms are usually so well controlled that the bronchial mucus is gradually expectorated. Moreover, the necessity of repeated instillations of iodized oil usually indicates that undiscovered or uncontrolled allergies demand further study and treatment.

(f) The intravenous administration of neoarsphenamine exerts spectacular relief in a few cases of severe bronchial asthma. It is especially indicated when a greenish abundant sputum containing spirochetes is present, but the drug in certain cases seems to exert a nonspecific effect apart from its bactericidal action. Beneficial effects from the intravenous administration of calcium gluconate or calcium chloride have not been

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12. Graesser, J. B., and Rowe, A. H.: Inhalation of Epinephrine for the Relief of Asthmatic Symptoms. *J. Allergy* 6: 415 (July) 1935.
13. Maytum, C. K.: Bronchial Asthma: Relief of Prolonged Attack by Colonic Administration of Ether. *N. Clin. North America* 15: 201 (July) 1930.
14. Balyeat, R. M.; Seyler, L. E., and Shoemaker, H. A.: The Diagnostic and Therapeutic Value of the Intratracheal Use of Iodized Oil in Cases of Intractable Asthma. *Radiology* 24: 393 (March) 1935.

evident in my work. In severe asthma the intravenous use of sodium iodide may be of temporary help. Its use should always be preceded by oral administration to rule out a possible allergy thereto.

(g) The fact that bronchial asthma may disappear or decrease during certain infections has led to the use of fever therapy with varying benefit. In resistant asthma, such fever may be induced by intravenous injections of typhoid bacilli or by heat therapy. I have resorted to such therapy in a very few cases. The benefit of roentgen therapy is uncertain and should never supplant the therapeutic recommendations as outlined in this paper.

(h) Breathing and other exercises as developed especially in England¹⁵ are of value when deformities or underdevelopment of the chest and its musculature have arisen from chronic asthma. With the control of such asthma, however, with therapy based on existing allergies, indications for these exercises decrease.

(i) A warm dry climate, especially in high altitudes, seems to decrease allergic reactions to foods and also to certain inhalants, but with proper recognition and control of allergenic causes such climatic change is unnecessary. The idea of curing asthma by climate is futile and often leads to financial ruin.

(j) Intractable asthma becomes less frequent with proper diagnosis and treatment. However, until allergenic causes are controlled and mucus is expectorated, an emergency may exist. Such severe cases should be hospitalized in environmentally controlled rooms, foods on elimination diet should be given and immediate attention should be paid to other possible allergenic factors. The frequent use of epinephrine hypodermically is most necessary. Dehydration often exists, increasing the inspissation of bronchial mucus. Benefit, therefore, may arise from intravenous saline and dextrose therapy. The contraindication for morphine and other sedatives has been noted. If the circulation will permit, induced vomiting by ipecac or apomorphine hydrochloride may aid in the expulsion of bronchial mucus. Theophylline with ethylenediamine,¹⁶ 7½ grains (0.5 Gm.) in 10 cc. by vein, may give rapid relief in cases resistant to epinephrine. Kahn¹⁷ also recommended the slow administration by vein of from 1 to 3 minims (0.06 to 0.2 cc.) of a 1:1,000 solution of epinephrine. Oxygen therapy or helium and oxygen¹⁸ may be advisable. In selected cases anesthesia with ether in oil by rectum¹³ has been a life saving measure.

(k) Rest as in other chronic diseases must be utilized in many cases, according to the patient's problem. Circulatory exhaustion and mental and physical fatigue thereby are benefited. It is best carried out in a hospital or sanatorium, though, if the necessary dietary and environmental control can be provided, financial considerations may require such rest at home.

(l) Of greatest importance is the unquestioned cooperation of the patient over a long period. Relief may occur rapidly, but diet control and hyposensitization often must be continued for months and frequently for years if lasting results without further treatment are to occur.

CONCLUSIONS

1. Excellent or good relief has resulted from available diagnosis and treatment in approximately 80 per cent of patients suffering with bronchial asthma. Inhalant and food allergies are the usual causes, bacterial allergy being of minor importance.

2. Carefully recorded histories often suggest the allergic etiology. Moreover, the causes of wheezing other than bronchial asthma must be remembered.

3. Positive cutaneous reactions must be checked by history and clinical trial. Often they are of potential or nonspecific significance.

4. Because of negative cutaneous reactions not only to food but also to inhalant allergens, supplemental methods of diagnosis must be used, such as trial diets, diet diary, leukopenic index, ocular or nasal tests and environmental control.

5. Elimination diets for the study of possible food allergy require absolute cooperation and assured protection of nutrition and of optimal weight.

6. Treatment of inhalant allergy necessitates hyposensitization with proper antigens and environmental control according to the problem.

7. Food allergy demands elimination of the allergenic foods until tolerance returns. Hyposensitization with food allergens is not generally successful.

8. For relief of symptoms the iodides, epinephrine by hypodermic injection or inhalation, ephedrine by mouth and intrabronchial iodized oil in selected cases are of greatest value. Nasal surgery for removal of obstructions and actual infection should be done only after careful study and control of causative allergies.

9. Intractable or severe asthma requires the use of environmental control and elimination diets, while other indicated procedures such as intravenous saline solution and dextrose, repeated hypodermic injection of epinephrine and possibly oxygen, helium and oxygen therapy or other measures are being utilized. Theophylline with ethylenediamine by vein may give relief in cases resistant to epinephrine. As in all bronchial asthma, morphine is contraindicated.

10. Finally, for lasting satisfactory results, continued study, treatment and cooperation are demanded for months and often for several years until all allergenic and secondary causes of bronchial asthma are recognized and controlled.

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ABSTRACT OF DISCUSSION

DR. CHARLES H. EYERMANN, St. Louis: We have heard an excellent summary of the methods of therapeutics and of diagnosis applicable to bronchial asthma, an affliction which in the past forty years has emerged from the welter of neurosis as a disease based on allergy. The experiences of other physicians with these methods would most likely agree when the relevant fundamental principles are involved, but, owing to the comparative youth of the concept of allergy and to the difficulties of the clinical problem, there will be differences of opinion as to the details of their application as well as to the interpretation of results. The utility of the diagnostic and therapeutic measures enumerated by Dr. Rowe in general depends on one's personal clinical judgment. Because of the practical implication, bacterial allergy as a cause *per se* of bronchial asthma is a moot question. My experience agrees with that of Dr. Rowe in that the absorption of bacteria or their products as a cause of allergic asthma is a rare clinical entity. That patients will wheeze from secretory obstruction of the tracheobronchial tree from which bacteria can be cultivated is undeniable, but that is not allergic asthma. That the absorption of bacteria or their products may produce bronchial edema or spasm is contro-

15. Bray.³

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18. Barach, A. L.: The Therapeutic Use of Helium, *J. A. M. A.* 107: 1273 (Oct. 17) 1936.

versal both experimentally and clinically and as far as my experience is concerned is a rarity, attested by the infrequency with which bronchospasm follows the parenteral injection of bacterial vaccines. The combined good and excellent results are gratifying and merit commendation but provoke comment. In view of the fact that 86 per cent of good and excellent results are obtained in the age group 0 to 15 years and that males are likely to lose their asthma at puberty, it is pertinent to inquire the percentage of males in this age group. It is also important to know how much less asthma one must have in order to obtain a good or excellent result. These words connote a personal standard and will not be interpreted by all observers in the same manner. To express the results of treatment, it has seemed simpler to compare the number of asthmatic episodes during and following specific treatment with those without or before specific treatment was instituted. Remissions for five years and longer are not infrequent. Such a period of freedom from asthmatic episodes would be my interpretation of an excellent result. Clinical studies like this one of Dr. Rowe's will aid in the eventual simplification of a complex clinical problem.

DR. GEORGE PINESS, Los Angeles: The question of food sensitivity as discussed by Dr. Rowe appears to be the major factor in the production of allergic diseases, particularly bronchial asthma. As a matter of fact, in a study of several thousand individuals who were studied physically, by laboratory, roentgenologically and from an allergic standpoint, only 1 per cent were sensitive to foods and foods alone. This was not limited to any particular age group. Seventy per cent were multiple sensitive, foods being one of the factors involved. On the other hand, Dr. Rowe in his own statistical studies reveals a sensitivity of 40 per cent of his individuals to pollen and another 40 per cent sensitive to inhalant or epidermal or environmental types of allergens. The fact is that multiple sensitivity is a rule, and food sensitivity may be a part of it and may be a factor in the production of bronchial asthma but does not occur as frequently as Dr. Rowe would lead us to believe. The question of the comparative value of skin testing with trial diet brings up a controversy that occurs at every meeting. It is my opinion that, if cutaneous testing is done on a sensitive individual with active proteins or allergens, positive skin reactions will be obtained and generally clinical proof of this sensitivity is obtainable. That the percentage of positive reactions in many individuals is great does not preclude their specificity. The positive reaction always indicates an at least potential possibility of its being a cause of the allergy. However, it takes more than cutaneous testing to diagnose and cure allergic individuals and in my opinion cutaneous testing is not a means to an end to make a diagnosis but merely to determine cause after that diagnosis of allergy has been made. It takes skill and intelligence to make an analysis of the problem, and when the clinical history is corroborated by cutaneous testing there is some value to the tests; but merely to use it to advise individuals of their sensitivity to this or that and have them eliminate these items from the diet or environment does not give a patient anything of value and throws a perfectly good work out of repute. The trial diet question is not a new one, and it has always been my belief that the patient's guess is much better than the doctor's. When one takes a diet of twenty or more foods, it is very difficult for the clinician to guess which food might be a factor. Not alone that but there are many other factors that are important. One cannot determine clinical sensitivity in an hour or in several hours or sometimes in a month, because the patient's limit of tolerance is something for which no yardstick exists.

DR. JOHN FRANCIS QUINLAN, San Francisco: Some aspects of asthma are comparable to the degenerative diseases. Physiologically it is a spasm of the bronchioles which, like the intestine and the vascular system, are encircled by smooth muscle. Spasm is merely a sustained anaerobic phase of contraction in the cycle of muscular activity. Allergens are characterized by the benzene ring; plant tissues contain the phytosterols; animal tissues, including hair and feathers, cholesterol; and dusts, both. Proteoses contain amino acids, which have the benzene ring as their nucleus. Coal and oil, the basis of many medicaments, are the lipid residue of prehistoric vegetations. Asthmatic patients

are emotionally unstable. Emotional instability is accompanied by a faulty dextrose metabolism. Dextrose, which relieves asthmatic patients, is essential in the aerobic phase of muscular relaxation. Adrenal cortex extract, controlling the retention of sodium in the body, determines consequentially the hydration of the tissues and the disposition of dextrose and the other electrolytes. An increase of potassium, a result of dehydration, is characterized by spasticity. Precancerous tissue, being deficient in glycogen, does not stain with iodine. Senile vaginal tissue is deficient in glycogen. Senile vaginitis is curable by the gonadal extracts, which means that they are involved in the fixation or condensation or polymerization of dextrose in the tissues. Hypertension, claudication, angina pectoris equivalents for vascular spasm, and asthma are aided by gonadal extracts, which means that they are involved with dextrose in muscular relaxation. Sterols, conjugations of the benzene ring and the mother substances of the gonadal and cortical extracts are comparable to the glucosides of digitalis and strophanthus. The adrenal cortex and gonads are concerned with the dynamism of the body. The gonads are considered endocrine glands, though their glandular structures are continuous with their excretory ducts, the apparent separation of the ovary serving the purpose of conservation of the dynamic factors in the follicular fluid, which is discharged into and resorbed from the abdominal cavity as the ovum is extruded into the oviduct. The excretions of the testes are physiologically released in the orgasm at intercourse. They stimulate, through absorption from the vagina, follicular development and supply chemicals which are essential for the maintenance of a woman's emotional composure and physical energy. Any interference with their normal deposition in the vagina directly conditions the emotional state, which, depending on the woman's basic character, determines the development not only of asthma but also, more remotely, of a degenerative disease.

DR. JULIAN COHN, Los Angeles: I should like to discuss a better classification of allergy in its relation to everyday life. Drs. Coca and Cooke in 1922 and again in 1934 discussed allergy in two different forms. The first, the normal allergies, such as hypersensitiveness of infection which anybody may acquire, and abnormal forms, such as bronchial asthma, hay fever and related conditions, are based mainly on inheritance. If these two forms are understood, a better understanding will prevail. A review of the literature of those reporting relief of asthma in their series has shown that all the cases belong in four groups. For instance, 25 per cent are practically cured, 25 per cent obtain moderate to great relief, 25 per cent obtain slight relief and 25 per cent obtain no relief. I would emphasize from the point of view of the allergist that scratch testing elicits a small percentage of positive tests. To get any type of reaction at all, patients must be very sensitive. The intracutaneous method of testing is the only adequate method. The number of diagnoses of pollen asthma cases may be materially increased if the work of Peshkin is followed. He instilled a small amount of dry pollen in the conjunctival sac. It serves to prove the diagnosis obtained by cutaneous testing. If this is done, more cases will be diagnosed than are diagnosed now. To illustrate, a young man came to Los Angeles and contracted asthma. He went to an Eastern clinic, was tested and told to forget it. He returned to Los Angeles. In testing him I could find no causative factor. The ophthalmic test with the pollen was done and reactions to grasses and weeds were obtained. Therapy was effective. As Dr. Rowe said, morphine is really contraindicated in severe asthma, but occasionally one will find a case in which one has to use it. Negativistic attitudes of physicians who speak of poor results should be dispelled. There is no justification for it. Climatic change may do good in some but not in a large number of cases.

DR. ALBERT H. ROWE, Oakland, Calif.: Dr. Eyermann's opinion that bacterial allergy infrequently is a major cause of bronchial asthma confirms the general conclusion. I agree, moreover, that occasionally wheezing and other symptoms suggestive of bronchial asthma may arise from bronchial infection alone and not from sensitization to the causative bacteria. Dr. Eyermann was correct in stating that conclusions drawn from my statistics could vary according to the manner of their analysis. However, as presented, they demonstrate without question

that excellent or satisfactory relief is available for the large majority of patients suffering with bronchial asthma, provided the methods of diagnosis and treatment available today as presented in this paper are properly utilized. Dr. Piness questions the use of trial diets again. My continued experience during the last fifteen years demonstrates that the use of such diets, especially the elimination diets, as a diagnostic measure reveals much food allergy that otherwise is difficult to recognize. Adequate amounts of protein, vitamins and calories must be insisted on when such diets are used, absolute cooperation and accuracy on the patient's part must be had, and under no circumstances should elimination diets be continued if nutritional damage or undesirable loss of weight cannot be prevented. My experience has repeatedly indicated that scratch tests with food allergens fail to reveal many foods to which allergy exists and that intradermal testing with such foods may give reactions which are not indicative of clinical sensitization and also may fail to reveal certain foods productive of low grade or chronic allergic disturbances. Thus diet trial modified as discussed in my paper seems necessary for adequate study of many patients suspected of food allergy. My statistics demonstrate that inhalant allergy has received as much consideration in my treatment as has food allergy, if not more. They also show that multiple sensitization to foods and inhalants is the rule, though a definite number of patients suffer with asthma from food or inhalant allergy alone. Dr. Cohn's warning about the intradermal test is important. Too many deaths have occurred from its initial use without preliminary scratch tests. His mention of the ocular test is valuable and serves to emphasize the fact that the cutaneous test may be negative not only to foods but also to inhalant allergens in certain cases.

SUPERVOLTAGE ROENTGEN TREATMENT OF CARCINOMA OF THE BLADDER

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The percentage of cures of advanced malignant disease by any of the therapeutic methods now in use is not high. This applies to new growths which are superficially located as well as to those which occur in the deeper tissues.

Recently a large number of cases of cancer of the skin was reviewed by one of us¹ with a view to determining the results of therapy, both surgical and radiologic, in relation to the size of the lesion. It was found that those epitheliomas which did not exceed 1 cm. in diameter showed 95 per cent cures by either irradiation or surgery. However, when the growth exceeded 2.5 cm. in diameter this figure fell to 50 per cent.

Advanced deep-seated carcinoma which is inaccessible and must be irradiated through a large volume of normal tissue may be expected to show even a less satisfactory response. Any method of treatment which holds some promise of cure of a small percentage of deep-seated new growths and which will cause regression, at least temporarily, with symptomatic relief in a larger percentage is worthy of consideration.

At the June 1937 meeting of the American Association of Genito-Urinary Surgeons a paper on the high

voltage roentgen therapy of malignant tumors of the urinary bladder was presented.² The results in twenty-four cases treated by the usual 200 kilovolt roentgen rays were set forth in this communication. There were only seven patients in this group whose therapeutic program was limited to external irradiation alone. Of these, five had growths classed as inoperable and one, although the growth was operable, refused surgery. Of the two favorable cases in this small group, one showed complete disappearance of two small papillary tumors near the orifice of the left ureter following 200 kilovolt irradiation through four portals, the dosage being pushed to the limit of skin tolerance. In the second case some regression was obtained of a moderately large papillary tumor involving the left lateral wall and trigon of the bladder. In an occasional case in the more advanced group it was felt that the amount of regression following external irradiation had been sufficient to place the patient more definitely in the operable class. The conclusions drawn from this study were as follows:

It is our belief that external irradiation with 200 kilovolt equipment by ordinary methods and with ordinary dosage has no place as a curative agent in the routine treatment of malignant tumors of the urinary bladder. As a palliative agent it will prove useful, especially in the arrest of hemorrhage, and in an occasional case sufficient regression may be accomplished to render an extensive lesion more amenable to cure by other means.

At the time of preparation of the manuscript on 200 kilovolt roentgen irradiation of carcinoma of the bladder, a supervoltage roentgen therapy unit was put into operation at the Collis P. Huntington Memorial Hospital in Boston. This machine incorporates a new principle of roentgen ray generation, which has been described elsewhere in detail by its designers and builders, Dr. Robert J. Van de Graaff and Dr. John G. Trump of the Massachusetts Institute of Technology.³

The generator is of the electrostatic belt-conveyor type. Negative electrons are supplied at approximately 10,000 volts to a series of six rapidly moving belts that travel from the ground to a high voltage terminal mounted on an insulator. The high voltage terminal may be charged to a negative potential of somewhat over 1,000,000 volts. This voltage is distributed to a multisectional porcelain tube of the cascade type by means of corona points. The tube is approximately 16 feet in length and extends through the floor of the generator room into the treatment room below. All roentgen radiation is produced at the lower end of the tube in a "transparent" anode of either lead or gold. The unit has a capacity of 1,000,000 volts at 3 milliamperes. This apparatus has been in use for the routine treatment of malignant disease since February 1937. It has proved to be exceedingly reliable in operation and delivers a very high radiation intensity which approximates in quality the gamma rays of radium.

The treatment of deep-seated neoplasms by the external application of radium in so-called packs and bombs is by no means a new or experimental procedure. The gamma rays of radium are the shortest, most penetrating rays available at present for cancer therapy.

From the Department of Radiology, Collis P. Huntington Memorial Hospital, Harvard University.

Read before the Section on Radiology at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 15, 1938.

A large number of the cases reported have been seen in private practice. We are appreciative of the interest and cooperation shown by those urologists who have referred these cases.

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However, the amount of radiation that can be delivered to a deep-seated tumor is dependent not only on the penetrating power of the rays but also on the distance of the source of radiation from the patient. The greater this distance, within certain limits, the greater the depth dose. Radium is available in such comparatively small quantities that its application at distances greater than from 10 to 15 cm. is not feasible because of the excessive length of time for the treatment. Supervoltage roentgen rays, on the other hand, are not only short in wavelength but can be produced in intensities equivalent to many hundreds of grams of radium, and therefore their use at distances of from 50 to 100 cm. becomes entirely feasible.

A brief review of the physical characteristics of roentgen rays produced at 1,000,000 volts constant potential as compared with those generated at 200 kilovolts will aid in an evaluation of their use in the treatment of malignant disease. One-fourth inch (0.64 cm.) of lead is considered sufficient protection from 200 kilovolt roentgen rays. It takes from $5\frac{1}{2}$ to 6 inches (14 to 15 cm.) of lead to absorb the direct rays produced at a constant potential of 1,000,000 volts.⁴ This is the amount of lead commonly used for protection from radium.

The approved method of expressing the quality of an x-ray beam is that thickness of copper which, when interposed between the source of radiation and an ionization measuring instrument, will reduce the intensity of the rays 50 per cent. This is known as the half-value layer. The half-value layer for 200 kilovolt roentgen rays is approximately 1 mm. of copper; the half-value layer for 1,000,000 volt roentgen rays is 10.5 mm. of copper.

The average human pelvis measures 20 cm. in its anteroposterior diameter. Thirty-two per cent, or approximately one third, of the amount of 200 kilovolt radiation delivered to the surface of the pelvis reaches its center. In other words, the 10 cm. depth dose for 200 kilovolt roentgen rays is 32 per cent. By varying the factors of filtration and distance, this figure can be raised slightly. The 10 cm. depth dose for 1,000,000 volt roentgen rays is 51 per cent. It is also possible to raise this figure slightly. Approximately 19 per cent more radiation per unit of surface dose can be delivered to a neoplasm at the center of the pelvis with 1,000,000 volt roentgen rays than is possible with 200 kilovolt rays.

There are two differences in the clinical response to 1,000,000 volt roentgen rays which are of great importance. First, the tolerance of the skin to shorter wavelengths is greater than it is to longer wavelengths. It takes twice as much radiation to produce erythema of the skin with 1,000,000 volt rays as it does with 200 kilovolt rays. Second, general malaise, nausea and vomiting, so-called roentgen sickness, are less at the higher voltage.

Whether or not there is a greater selectivity of the shorter wavelengths for new growths is still a question. Most experimental work points to the fact that it is the quantity of radiation delivered to a tumor rather than the quality that is important. However, many trained observers who for years have employed large amounts of radium for external treatment are convinced that the shorter wavelengths are more effective in the destruction of neoplastic tissue.

Preliminary experiments on the irradiation of *Drosophila* (fruit fly) eggs have been carried out in collaboration with Dr. John C. Larkin, resident in radiology at the Peter Bent Brigham Hospital, Boston. By using some medium, such as a box of rice or a block of pressed wood, which absorbs roentgen rays in the same degree as human tissue, it has been shown that 1,000,000 volt roentgen rays are approximately 10 per cent less effective than 200 kilovolt rays in killing the eggs on the surface, but in the depths conditions are reversed and the shorter wavelengths are more effective than ionization depth measurements would lead one to expect. This experimental work checks well with our clinical observations. In other words, the physiologic depth dose is greater than that determined by ionization measurement.

Unless a new growth is small and superficially located, the commonly accepted method of external irradiation is small daily exposures extended over a period of several weeks or perhaps months. For several years we have been treating large epidermoid cancers of the skin with daily fractionations of 200 kilovolt roentgen rays.⁵ It has been found that, if 200 roentgens a day is given, a total of from 4,000 to 5,000 roentgens is necessary to control such lesions. We believe that epi-

Immediate Results of Irradiation in Twenty-Six Cases of Carcinoma of the Bladder

	Cases	Per Cent
Regression either complete or so nearly complete that small remnants of tumor could be satisfactorily fulgurated or treated by implantation of radium	7	26.9
Partial regression of tumor with relief of symptoms of pain, frequency, hematuria, etc.....	9	34.6
No regression of tumor and little or no symptomatic relief (5 cases previously irradiated at 200 kv.)	10	38.4
Of seven patients previously treated at 200 kilovolts, only two showed a fair response to higher voltage therapy		

dermoid carcinoma situated elsewhere in the body should respond in a similar manner to similar doses. If smaller daily doses are administered, a correspondingly larger total dose must be given to obtain results. We have learned from our experience with 200 kilovolt radiation of deep-seated pelvic tumors that a total dose of 4,000 roentgens cannot be administered to the neoplasm at the rate of 200 roentgens a day. The limitation has not been the reaction of the deeper tissues, such as the bladder and intestine, but has been dependent on the limit of tolerance of the skin and on the marked roentgen sickness that follows the administration of large daily surface doses. These undesirable factors are eliminated when 1,000,000 volt rays are used. Because of the greater depth dose, the greater tolerance of the skin and the lessened roentgen sickness, a daily surface dose of 400 roentgens is well tolerated, and 50 per cent of this dose is delivered to the new growth. The total tumor dose no longer is dependent on the reaction of the skin but is now limited by the tolerance of the intestine and bladder.

Our experience with supervoltage roentgen rays has been limited to fifteen months. We have brought the tumor dose of deep-seated pelvic lesions to a total of 3,000 roentgens, with daily exposures of approximately 400 roentgens to the surface, without untoward effect on normal structures. With this amount of radiation, symptoms of rectal and vesical irritation develop, but

4. Dresser, Richard, and Cosman, B. J.: Million Volt Roentgen Ray Protection, *Am. J. Roentgenol.*, to be published.

5. Dresser, Richard, and Dumas, C. E.: The Treatment of Cancer of the Skin by Divided Doses of High Voltage Roentgen Rays, *Am. J. Roentgenol.* 36: 332-336 (Sept.) 1936.

usually the patient recovers promptly. It is our belief that this dose is not sufficient to control epidermoid carcinoma permanently, but we believe that a total of at least 4,000 roentgens in the region of the tumor, administered at the rate of 200 roentgens a day to the tumor, may eventually be attained with safety.

The immediate results in twenty-six cases of carcinoma of the bladder treated with a tumor dose of approximately 3,000 roentgens are herewith reported. These cases were all in the so-called inoperable group or were recurrent after operation. They have been chosen without selection, and a number of them were in the last stages of advanced malignant disease. In seven cases, or 26.9 per cent, regression of the tumor was either complete or so nearly complete that small remnants of the growth could be satisfactorily fulgurated or treated by implantation of radium. Partial regression with relief of symptoms of pain, frequency, hematuria and the like occurred in nine cases, or 34.6 per cent. Two of these patients had previously been irradiated at a lower voltage. There was no regression of the neoplasm and little or no symptomatic relief in ten cases, or 38.4 per cent. Five of these patients had previously been irradiated at a lower voltage. Of seven patients previously treated at 200 kilovolts, only two showed a fair response to higher voltage therapy, as shown in the accompanying table.

These results are better than those which we have been able to obtain with lower voltage radiation. The majority of the patients have had only a slight general reaction, and the local reactions, as a rule, have not been severe. The papillary tumors have responded rather more satisfactorily than the infiltrating type.

This method at its present stage of development is not to be recommended as a substitute for surgical excision or radium implantation in favorable cases. It is our belief that the total tumor dose is still too small to control epidermoid carcinoma permanently, but it is our hope that eventually an amount of radiation can be safely administered to neoplasms of the bladder which will result in the cure of lesions now considered hopeless from any other therapeutic standpoint.

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ABSTRACT OF DISCUSSION

DR. ROBERT S. STONE, San Francisco: I disagree with many statements that are being made about supervoltage irradiation. The question of depth dosage with supervoltage is a touchy one, because we talk about giving 200 roentgens to the surface, and that doesn't mean the same thing with the two different types of irradiation at all, so that one has to talk about surface dose when one is talking about depth dose, and one has to include the depth dose when one is talking about what one can give a patient. With regard to the question of skin erythema, I don't know that the roentgens we use in California and San Francisco differ from those used in other parts of the country, but the statement was made that one can give twice as much to the surface with supervoltage. I frequently have given 800 roentgens to the surface with 200 kilovolts at one sitting, and I certainly would not dare to double that with the other machine. So if one talks about skin erythemas one has to take into account the backscatter, the effects, and other elements. When the authors say that they were stopped by the cutaneous effects in using 200 kilovolts I wonder whether they were using 200 kilovolts at a long target skin distance and with a composition filter, or with 0.5 mm. of copper at 50 cm. They do not tell that. I think that if they use a longer target skin distance they will not be limited. With regard to the actual figures mentioned at the end of the paper on the improvement of supervoltage, it is difficult to compare any two sets of figures, and

I have none of my own that I would care to bring forward. On looking at Dr. Ferguson's figures published last year on 200 kilovolts at long target skin distance, one finds that he had twenty cases in 1936 that showed remarkable one year regressions, or 55 per cent, whereas in the present case he had seven cases, or 26.9 per cent. This would prove that 200 kilovolts is much superior to supervoltage if one uses 200 kilovolts at a long target skin distance and give it in small daily fractions. Radiologists have got to get away from the idea of bigger depth doses and confine themselves more to the rate of giving, the total time it takes to give it, and reaction of the tumor as the treatment is being given.

DR. L. H. GARLAND, San Francisco: The problem of the relative efficiency of different voltages in the handling of a disease which is so often incurable appears to tax our judgment. The authors believe that one can give twice as many roentgens to the skin with a supervoltage unit as one can with a 200 kilovolt unit; that is, that supervoltage is only half as efficient as orthovoltage in the production of damage to the skin. On the other hand, they believe that supervoltage has twice as good an effect on the tumor at a depth of 10 cm. Now, if supervoltage is twice as destructive to the epithelial cells in the bladder tumor, it should also be twice as destructive to the epithelial cells in the skin. Having the privilege of observing patients treated by two different supervoltage units in this city, I have the distinct impression that the main advantage of a supervoltage unit lies in the large quantities of x-rays that it produces per minute, in comparison with the orthovoltage unit. Patients may therefore be treated with supervoltage units at a longer distance or in a shorter time than with ordinary units, a gain of a little time and not a gain of biologic efficiency. There is absolutely no proved cancericidal superiority of 400 or 800 kilovolt x-rays over 175 kilovolt x-rays. Stone (*Radiology* 30:88 [Jan.] 1938) has emphasized that it is not the tolerance of the skin which is the limiting factor in adequate dosage of deep-seated tumors, using ordinary 200 kilovolt x-rays, but it is tolerance of small bowel epithelium and neighboring normal structures. Other factors, such as the daily dose, the total time of treatment and perhaps the intensity (roentgens per minute rate), are probably much more significant as regards improvement in results from radiation therapy than mere voltage. I have a patient with carcinoma of the bladder, clinically arrested for eleven years with 200 kilovolt irradiation alone. The lesion was recurrent subsequent to operation, affording material for biopsy. This, of course, is a very fortunate and unusual event. It is well to remember that about ten years ago papers were presented to this section of the American Medical Association extolling the virtues of 200 kilovolt irradiation over 140 kilovolt irradiation. Now, 800 kilovolt irradiation is fashionable. In ten more years doubtless 10,000 kilovolt irradiation will be the magic weapon. I do not wish to disparage the usefulness of roentgen irradiation in palliating and at times controlling bladder carcinoma; I merely wish to disparage giving undue credit to supervoltage. Irrespective of the voltage which one uses in the treatment of these tumors, it is of utmost importance that they be centered properly. It is wise to check one's centering occasionally by roentgenograms made on the roentgen therapy table, with just a few cubic centimeters of sodium iodide in the bladder.

DR. HENRY J. ULLMANN, Santa Barbara, Calif.: Unfortunately, I haven't got a supervoltage machine to use. But I do not feel that it is fair to report cases in which the time has been so short that there is simply palliation. I have had a patient for two years now who had a carcinoma of the bladder, who was treated at 200 kilovolts, with filtration of 2 mm. of copper, 71 cm. distance, treated simply fore and aft, only two ports, over a period of four months, and a urologist reported only a short time ago that there was no trace of carcinoma. Now that is not important to cure; that is palliation. I have yet to see a carcinoma of the bladder that is not benefited, at least temporarily.

DR. JOHN T. MURPHY, Toledo, Ohio: I want to defend the authors in reporting this series of cases, because I asked them to do it. I wanted just this discussion. For the benefit of those men who have a machine of only 200,000 volts, and I

have one machine of higher voltage than that, I want to say that I am treating all my carcinomas of the bladder and prostate with 200 kilovolts. I tried 400 kilovolts at the usual technic, which has never exceeded 200 roentgens a day, with a heavy filter, and I found that the permanent results were not any better than previously, and the patient's symptoms were not so good during treatment. The last year I have been using the so-called 'Ferguson technic' at 1 meter with a relatively heavy composition filter, with 100 roentgens a day, 4 roentgens a minute, one field treated daily, five fields, 3,000 roentgens per field. I have no cured cases of either. I have, however, been able to do what doctors should always try to do: have alleviated the symptoms.

DR. RICHARD DRESSER, Boston: I anticipated some difference of opinion and I have not been disappointed. Regarding the size of the field, I agree with Dr. Stone. If one employs large portals, 20 by 20 cm., there is little difference in the depth dose as measured with a thimble ionization chamber. However, I think it bad practice to use a 400 square centimeter field in order to increase the depth dose when the disease-bearing area may be included by a smaller portal. The use of large fields necessitates the irradiation of much normal tissue, which may cause unnecessary damage. With 1,000,000 volt roentgen rays it is possible to limit treatment to a small disease-bearing area without affecting the depth dose. With regard to our 200 kilovolt technic, we have employed long distances up to 80 cm. We have given daily doses varying from 300 to 600 roentgens, depending on how well the patients tolerated the treatment. The results of 200 kilovolt therapy which Dr. Ferguson reports are better than those which we have been able to obtain. In reporting this series of cases, in which the treatment has been recent, we have not claimed any cures. However, regression of disease and palliation have been more pronounced than with our 200 kilovolt technic. Supervoltage roentgen radiation has been branded as experimental, but let us suppose that one could acquire 1,000 Gm. of radium, which would enable him to treat at a distance of from 70 to 80 cm. Such a procedure would not be considered particularly experimental. Yet this would represent essentially the same type of therapy that is being administered with 1,000,000 volt roentgen rays. In other words, the object of the use of supervoltage roentgen apparatus is to produce a type of radiation which is equivalent or nearly equivalent to the gamma rays of radium and in amounts sufficient to allow the employment of a long focal skin distance. The amount of radiation delivered to a deep-seated tumor is therefore much greater than it is possible to give with amounts of radium now in ordinary use. Shall we be treating at 10,000,000 volts a few years from now? I do not know. I think we should be satisfied with 1,000,000 volts for a while until we have found what may be obtained in the way of end results. It is the opinion of a number of physicists that, should the necessity arise, it will be mechanically possible to produce roentgen rays at 3,000,000 volts or more.

The Infinitesimal Currents of Nerve Centers.—Neurophysiology is today one of the most active fields of hyphenated science. The techniques are becoming increasingly refined. A century and a quarter ago it was an epoch-making discovery to make a simple distinction between the sensory and motor roots of the spinal cord. Today the almost infinitesimal currents of nerves and nerve centers are registered, their rhythms photographed in curves of beautiful precision. With devices for both auditory and visual magnification, the electrometry of the brain has swiftly amassed voluminous data—more in fact than the investigatory cerebrum can immediately cope with. By the method of thermocoagulation, individual layers of the brain cortex are being separately explored. By means of ultra delicate probing, microscopic groups of nerve cells are being identified in the medulla. Such researches are destined to give us an intimate knowledge of the architecture of the nervous system, and this knowledge will make our concepts of human behavior more deterministic and mechanistic in the best scientific sense.—Gesell, Arnold: *Scientific Approaches to the Study of the Human Mind*, *Science* 88:225 (Sept. 9) 1938.

Clinical Notes, Suggestions and New Instruments

THE BLOOD SUGAR AND CARDIAC INVOLVEMENT IN RHEUMATIC FEVER

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The rarity of rheumatic heart disease in diabetic patients is significant. Several authors have made references to the infrequency of the development of the former condition in these patients. In a study of fifty-eight cases of active rheumatic heart disease, I have been impressed by the high blood sugar tolerance and low blood sugar curve found to be present in many of these patients.

Joslin¹ observed only six cases of acute rheumatic fever in approximately 6,000 cases of diabetes during the course of twenty-nine years. He said: "Rheumatic heart disease is of extraordinary rarity. In 1917 I could recall no case of diabetes under fifty years of age in which the patient complained of shortness of breath or presented the signs of an incompetent heart due to valvular disease of a definite and unquestionable rheumatic origin. In a series of fifty-six autopsies performed on young adult diabetics, only one case of rheumatic heart disease was found."

Howard F. Root² wrote in part: "Strangely enough, in the ten years from 1920 to 1930 rheumatic heart disease was not encountered in diabetic autopsies at the Deaconess Hospital. Since then there have been five or six cases among two hundred diabetic autopsies."

Joseph H. Barach³ wrote: "In my group of 350 cases of diabetes, a history of rheumatic fever was obtained in thirty-seven patients. These thirty-seven cases of rheumatic fever occurred prior to the development of diabetes. In no case have I seen acute rheumatic fever in a diabetic. Valvular disease of the heart develops in more than half of the patients having rheumatic fever. Under such conditions, in the thirty-seven diabetics who had rheumatic fever we should have found valvular disease of the heart in eighteen or nineteen cases. It is therefore highly surprising to note that in these thirty-seven patients only one case of valvular disease was discovered." Barach concluded: "One may deduce from these observations that when rheumatic fever attacks an individual who is a potential diabetic, or rather one who is destined to become diabetic, such a patient's heart will be comparatively immune to endocardial involvement."

As the specific cause of rheumatic fever is unknown and its treatment unsatisfactory, progress in the treatment of the disease process and in the solution of its etiologic factor would be made were we able to discover or create a condition in the body which would be inimical to the infection.

From the observations of the authors quoted it may be indicated that diabetes mellitus is a body state which protects the individual from cardiac involvement in the event of his contracting rheumatic fever. If this is a fact, is the protective influence due to hyperglycemia, to undetected periods of acidosis, or to something in the secretions of the pancreas, liver or endoerines?

If the hyperglycemia in the diabetic patient exerts a protective action against cardiac involvement, it would be expected that individuals who are susceptible to, or those who contract rheumatic heart disease would have a low or flat blood sugar tolerance curve and therefore a high sugar tolerance.

From the Medical Services of the Municipal and Mount Sinai hospitals. The blood sugar determinations in the series of eleven children were made at the Mount Sinai Hospital, New York, through the courtesy of Dr. Samuel Karelitz on the service of Dr. Bela Schick.

1. Joslin, E. P.: *The Treatment of Diabetes Mellitus*, ed. 6, Philadelphia, Lea & Febiger, 1937.

2. Root, Howard F.: Personal communication to the author, Oct. 22, 1934.

3. Barach, Joseph H.: *The Incidence of Rheumatic Heart Disease Among Diabetic Patients*, *Am. Heart J.* 2: 196-201, 1926-1927.

Holsti,⁴ in his research on patients with acute or chronic lesions tested with 100 Gm. of dextrose in 300 Gm. of water, confirmed the upset in the balance of the internal secretions in these conditions. In several cases there were indications of symptomatic hyperthyroidism, and, in a few, alimentary or even spontaneous glycosuria indicated derangement of pancreatic function. In still others the glycemia was of the hypothyroid type.

McCulloch⁵ stated that all cardiac children of the type who have abdominal pain and vomiting associated with myocarditis have a low blood sugar content.

In an attempt to evaluate the relationship of the blood sugar content and cardiac involvement in acute rheumatic fever, I determined the blood sugar tolerance in cases of rheumatic fever and active rheumatic heart disease.

Thus far only fifty-eight such examinations have been made in fifty-eight patients with active involvement. This series of cases is not large but is interesting, and this preliminary report is made with the hope that further and more widespread study of this apparent relationship be undertaken by others with a larger material at their disposal.

Blood sugar tolerance was studied in forty-seven adults and in eleven children. In the former group the age limits ranged from 20 to 45 years, in the latter from 4 to 11 years. A series of thirteen control cases was used.

In the adults there was no case of acute rheumatic fever, but there was definite evidence in each patient of active endo-

Results of Tests

	Fast- ing	½ Hr.	1 Hr.	2 Hr.	3 Hr.
Adults					
Low curves: average of 24 cases....	76	99	91	83	...
Higher curves: average of 23 cases..	82	171	145	113	...
Average reading in 47 cases.....	79	135	118	93	...
Children					
Low curves: average of 9 cases.....	69.5	90	86	83	79
Higher curves: average of 2 cases...	110	173	195	168	143
Average reading in 11 cases.....	89.5	134.5	138	131	111
Average of 58 cases.....	80.9	134.8	121.8	121.3	...
Average of 13 control cases.....	85	155	112	87	...

cardial involvement due to rheumatic fever. This was proved by history, physical examination and laboratory evidence. The eleven children had acute rheumatic fever at the time the blood sugar determinations were made. The thirteen controls were adults and children with conditions other than diabetes or heart disease. One hundred Gm. of dextrose was administered for each test and the results were recorded in milligrams per hundred cubic centimeters of blood.

SUMMARY AND CONCLUSIONS

A review of the literature shows that rheumatic heart disease is but rarely encountered in patients having diabetes mellitus. A study of the blood sugar tolerance in a small series of patients with rheumatic heart disease and rheumatic fever indicates the desirability of further investigation as to this relationship.

Attention must be directed to the significant fact that nine of the eleven children with rheumatic fever had a flat blood sugar tolerance curve.

Blood sugar determinations should be made in all patients with acute rheumatic fever. If this percentage of flat curves holds true in a larger study of such cases, it would call for the administration of large amounts of dextrose to determine the effect, if any, on the course of rheumatic fever and its cardiac complications.

Dextrose may play an important role in preventing rheumatic heart disease in patients with acute rheumatic fever who have a low sugar tolerance curve.

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Special Clinical Article

THE TREATMENT OF TUBERCULOSIS UNDER THE GUIDANCE OF ORGANIZED MEDICINE

THE PENNSYLVANIA PLAN FOR TUBERCULOSIS
CLINICAL LECTURE AT SAN FRANCISCO SESSION

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The Pennsylvania plan for tuberculosis has two interdependent parts. The first is the striking of a balance between case finding, case treatment and rehabilitation. The second is the coordination of all groups engaged in the tuberculosis fight, first, through the establishment of a clear understanding on the part of all groups of the obligations and necessary limitations of each group, and, second, through a tuberculosis organization within organized medicine to act as a force to coordinate all groups, to take the initiative in setting standards for case finding, case treatment and rehabilitation and to work for the meeting of those standards by means which will be elaborated presently.

The organization consists of (1) a tuberculosis committee in every county medical society, (2) a tuberculosis committee in every state medical society and (3) a tuberculosis committee in the American Medical Association (not yet achieved). The first is coordinated by the second and the second by the third.

I. CASE FINDING

A. Education of the Public.—Education of the public is the great field of the National Tuberculosis Association and its component societies. Since its beginning near the start of this century it has been doing a great job in spite of unorganized opposition or indifference on the part of organized medicine, and to it belongs the greatest credit for the past drop in the death rate for tuberculosis.

To educate the public requires a great amount of money. Administrators of broad intelligence and administrative ability are necessary to carry on a great teaching movement; just as the quality of the faculty determines the quality of a college, so has the quality of the work of the National Tuberculosis Association and its component societies depended on the excellence of the personnel. The National Tuberculosis Association has been able to raise the necessary funds by selling Christmas seal stamps. It should be recognized by every physician that that money should be spent for education of the public, not for treatment of tuberculosis. Wrong views on this subject have led to subterfuge in some areas, which in the long run have been detrimental to the National Tuberculosis Association. This has been the fault of physicians in lacking an organization within organized medicine to support staunchly the National Tuberculosis Association in the field in which it is the master and to be responsible for the enlightenment of physicians, from whom in the past undiscriminating criticism has come.

In Pennsylvania, since adoption of the Pennsylvania plan there has been cooperation with the National

4. Holsti, Ö.: Blood Sugar with Articular Rheumatism, *Finska läk-sällsk. handl.* 66: 78-105 (Jan.-Feb.), 217-245 (March-April) 1924.

5. McCulloch, Hugh, in discussion at Round Table Conference on Heart Disease, *J. Pediat.* 5: 565 (Oct.) 1934.

From the Medical Society of the State of Pennsylvania.
Read in the Medical Division of the General Scientific Meetings at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 14, 1938.

Tuberculosis Association and its component societies, and this has been of tremendous advantage to the public, organized medicine and the National Tuberculosis Association. In Philadelphia the benefit has not been limited to tuberculosis. The experience and organized facilities of the Philadelphia Health Council and Tuberculosis Committee, the local component society of the National Tuberculosis Association, have been freely extended to advance many activities of the Philadelphia County Medical Society. Before organized medicine cooperated to fight tuberculosis, these bodies were enemies, to their mutual disadvantage and to the great detriment of the public.

B. Education of the Medical Profession.—1. Education of the Medical Profession in the Medical School: The American College of Chest Physicians has had functioning during the last several years a Committee on the Teaching of Chest Diseases in the Medical Schools, which has been working with the deans of all accredited medical schools to improve the teaching of diseases of the chest. It is a lamentable fact that there is no uniformity in the time devoted to this subject, and many medical schools do not even have a course in diseases of the lungs taught by a specialist in such diseases.

2. Education of the Medical Profession in the Practice of Medicine:

(a) The *American Review of Tuberculosis*, the finest and most comprehensive scientific publication on tuberculosis for the chest specialist and research worker, is published by the National Tuberculosis Association.

(b) *Diseases of the Chest*, a practical monthly journal on pulmonary disease, features early diagnosis and the modern treatment of tuberculosis. It is part of the Pennsylvania plan to have this journal go to every practicing physician every month. The circulation is now 10,000 monthly. The articles are written by specialists on pulmonary diseases primarily for general practitioners, who find most of the cases of pulmonary tuberculosis.

(c) Tuberculosis abstracts are furnished by the National Tuberculosis Association to all medical periodicals for reprinting and to physicians on request.

(d) Tuberculosis programs and papers for every variety of medical meeting are fostered by cooperation of the county medical societies' tuberculosis committees with the corresponding committee of the state medical society, with the National Tuberculosis Association and its component societies and with the American College of Chest Physicians. It is necessary to have whole hearted cooperation between all of these organizations to secure delivery of the greatest possible number of excellent papers on tuberculosis before the maximum number of medical meetings.

C. Education of State Legislators.—As large sums of money must be appropriated by the state legislative assembly to fulfil all parts of the Pennsylvania plan, it is necessary that all members of both houses of the state legislature be informed on that plan and kept fully cognizant of progress under it. To accomplish this purpose, the tuberculosis committee of each county medical society is made responsible for keeping in close instructive contact with every state representative and senator in the county. The informative procedure should cover the needs of the state in case finding, case treatment and rehabilitation. Similar responsibility rests on each member of the tuberculosis

committee of the state medical society for every legislator in his councillor district. This work must be carried on in close cooperation with the legislative committee of the state medical society. To secure this cooperation, the legislative committee of the state medical society must be kept fully informed by the tuberculosis committee of the state medical society of all of the legislative necessities under the Pennsylvania plan.

D. Method and Proper Cost of Case Finding.—Opinions vary widely concerning the best methods of case finding and the proper cost of case finding. The two are linked indissolubly. To a large extent the difference in opinion is due to the fact that a method which is effective and economical in an area with a low incidence of tuberculosis may be ineffectual and extravagant in an area where the percentage of persons with a positive reaction to tuberculin is high. Likewise a method satisfactory for one age group is not suited for all age groups. Therefore, under the Pennsylvania plan we recognize the following principles of case finding:

1. The least expensive practical method of case finding in public health work is the maintenance of a constant follow-up in the home by nurses specializing in tuberculosis of persons who have been in contact with patients known to be tuberculous or persons who have died of tuberculosis, together with the maintenance of thoroughly distributed tuberculosis clinics, out of which the nurse operates. The clinic should be properly housed and staffed with a competent tuberculosis specialist of excellent local reputation who is trained to perform artificial pneumothorax. The clinic should be equipped with fluoroscope and pneumothorax apparatus. Such a clinic will be able to hold the confidence of the local public and the confidence of local physicians, both of which are necessary for successful case finding. Tuberculosis is knowingly concealed by the patient's family and the family physician from incompetent and poorly equipped tuberculosis workers. Case finding is dependent on proper case treatment and is useless without it.

2. Testing with tuberculin should be followed by the taking of roentgenograms in cases in which the reaction is positive in (a) areas where the percentage of positive reactions is very low and in (b) special groups in which the incidence of active adult type tuberculosis is high.

In these special groups, such as the age group from 16 to 24 years, racial groups, slum area groups, certain occupational groups, and others in which the incidence of the active, adult type of tuberculosis is high, surveys with the inexpensive paper film method are applicable. There has been objection to this method in many areas on the part of organized medicine because of the belief that local roentgenologists or other physicians would be deprived of income. As a matter of fact, however, such surveys have led to increased case finding, with a consequent increase in work for both private roentgenologists and private physicians, in every area where they have been conducted.

The Pennsylvania health department under Dr. MacBride-Dexter has purchased two motorized x-ray field units, known as juvenile tuberculosis case finding units. These units are the last word in x-ray equipment and were designed especially for the department of health and approved by the Moore School of Engi-

neering of the University of Pennsylvania. They are so constructed that they can be dismantled, reassembled in the school or other building where the roentgenograms are made and then remounted on the trucks for transportation to the next town or city.

Each unit is accompanied by a trained roentgenologist and a technician and is sent into the counties for use with first year high school students in all schools of the state outside of Pittsburgh and Philadelphia. No child is examined without the consent of the parents, consent slips being sent out in advance. As the first step in the examination, the student is given the Mantoux test, and roentgenograms are taken of all those with a positive reaction. The films are sent at the close of each day's work in the field to the x-ray laboratory in Harrisburg, and the reports of the roentgenograms are sent to the parents and the family physicians.

It is interesting to note that in the first six counties visited by this unit in 1936 50 per cent of the parents consented to have their children given the Mantoux test. Of 37,485 ninth grade children examined in forty counties, 11.3 per cent gave positive reactions and approximately 155 showed symptoms of active tuberculosis.

Permission was requested from the superintendent of public instruction, which he readily gave, to take roentgenograms of the first year and senior students at the state teachers' colleges. Five hundred positive reactions were found in these schools. These tests will help to prevent teachers who have tuberculosis from coming in contact with children in the public schools.

II. CASE TREATMENT

Organized medicine alone has the combination of (a) knowledge of proper modern treatment of tuberculosis, (b) power and influence, when properly organized, to establish such treatment in every state in the United States and (c) lack of fear of the effect of the use of such power on the income of the organization.

The Pennsylvania plan set-up, as operating in Pennsylvania, is as follows: A. Dr. Edith MacBride-Dexter, secretary of health of the Commonwealth of Pennsylvania, is the leader of the Pennsylvania plan. B. In cooperation with her there is a tuberculosis committee of the Pennsylvania state medical society, with twelve members, one from each of the twelve councilor districts of the state (a wise arrangement contributed by Dr. Frederick J. Bishop, president of the Pennsylvania state medical society). C. A tuberculosis committee has been formed in each of twenty-three county medical societies in the state, those counties containing 53 per cent of the population of the state.

The function of the state society tuberculosis committee is to coordinate the activities of the county society tuberculosis committees and to support the accomplishments of Dr. MacBride-Dexter's Pennsylvania plan.

Under the plan there have been established in sanatoriums (a) proper living quarters for the sanatorium physicians, with private cottages for the married physicians and their families, (b) at least one physician to fifty patients, (c) security in their jobs for the sanatorium employees, (d) salaries for physicians at least equal to those paid in the army and navy, with a rising scale, and (e) sufficient nurses, ward maids and orderlies to do the work of the institution so that the patients are not called on to do the work.

It is recognized by organized medicine and the progressive Secretary of Health, Dr. MacBride-Dexter, that patient labor in the sanatorium is not proper rehabilitation and that the necessity leads to abuses and bias of judgment on the part of physicians when work in the sanatorium has to be done by patients and some patients must be selected to work in order to get the work done. Rehabilitation must come after cure, not during cure, in a sanatorium maintained to furnish rest, the primary cure for tuberculosis. Having sick patients work is false economy as well as being destructive of human life.

Under Dr. MacBride-Dexter, Pennsylvania has engaged in a huge tuberculosis sanatorium building program.

Organized medicine, with Dr. MacBride-Dexter, has secured a raise of approximately 50 per cent in the base pay of physicians in the state sanatoriums, together with a substantial increase in the pay of many of the other classes of sanatorium employees.

The practice of examining patients fluoroscopically before every pneumothorax refill, a very important reform, has recently been established. Fluoroscopic examination means so much in the avoidance of losing the pneumothorax collapse and in the avoidance of and the early detection of complications that it may be called the greatest guide to "pneumothorax judgment."

Patient labor is being abandoned as rapidly as finances will permit. The ideal is accepted and will be reached.

The tuberculosis clinic, as described under the heading case finding, will cost a great deal. Little has been accomplished in this connection. Organized medicine is working, however, with Dr. MacBride-Dexter to get the necessary personnel and equipment.

III. REHABILITATION

It is recognized that the rehabilitation of the tuberculous patient is in the early experimental stage. At the present time the patient, the sanatoriums and the public health organizations are suffering from the experiments on account of failure to recognize the following rules:

1. A patient should be cured before being rehabilitated. Rest of the diseased lung, of the body and of the mind is necessary and the only cure for tuberculosis.
2. The sanatorium is not the place for rehabilitation. The sick need the beds in the sanatorium; the cured patient can be rehabilitated more cheaply at home.
3. Rehabilitation should not place the cured patient in a position where the public is unduly menaced should reactivation of the disease occur.

All of my patients who are being rehabilitated by governmental agencies are being trained as "beauticians." They are not yet cured. Many are still receiving pneumothorax treatment. If their sputum becomes positive again they may take many of their customers back to the sanatorium with them. It would be almost as well to train them to be dietitians or chefs. It is hoped that when the Pennsylvania plan is further established in Pennsylvania the laymen functioning in rehabilitation schemes will be brought more into cooperation with the tuberculosis organization in organized medicine.

NOTE.—After this paper was written, the following letter was received from M. M. Walter, director of

vocational rehabilitation in the Department of Public Instruction of the Commonwealth of Pennsylvania:

June 6, 1938

My dear Doctor Burge:

It was very kind of you to give me a list of names of Chairmen of the County Tuberculosis Committees in this state. The information has been sent to all of our district offices with the suggestion that each one of the physicians be contacted as soon as possible and arrangements made to have all tuberculosis cases that may be eligible for the services of this Bureau, referred to us by the local committees. Furthermore, if possible, a plan will be worked out to have the chairmen act as examining physicians for us in determining the physical status of the clients.

You may be interested to know that several years ago a plan of cooperation was worked out with the State Department of Health, to have all the State Sanatoriums refer eligible cases upon discharge from such institutions, to the Bureau of Rehabilitation. At the present time, 28 arrested tuberculosis cases are being trained in schools and colleges under our supervision.

I assure you that the Bureau of Rehabilitation will be very happy to cooperate with your committees in the rehabilitation of any clients who are eligible for our services.

Cordially yours,
M. M. WALTER

R.

MMW:DR Director, Vocational Rehabilitation.

One should not forget the fiasco of rehabilitation of the veterans of the great war or the rackets that thrived under that cloak.

1930 Chestnut Street.

Council on Physical Therapy

THE COUNCIL ON PHYSICAL THERAPY HAS AUTHORIZED PUBLICATION OF THE FOLLOWING ARTICLE. HOWARD A. CARTER, Secretary.

THE EFFECT OF HEAT ON THE BLOOD VOLUME AND CIRCULATION

H. C. BAZETT, M.D.

PHILADELPHIA

The effect of heat on the blood volume and circulation is so familiar that it seems necessary to explain why it is being discussed again. It seems important, however, to stress certain controversial points that are less generally known and to contrast the effects of high temperatures applied in acute experiments or treatments of short duration with those of milder temperatures continued chronically for days. The mode of adaptation of subjects to mild temperatures (of the order that has to be endured in the summer in New York) may prove worthy of analysis for its clinical interest. Preliminary study seems to indicate that air-conditioned rooms should be added to the equipment of physical therapy departments. In such an analysis of the effects of heat it is necessary to distinguish the parts played by (a) local dilatation in the cutaneous vessels with its accompanying local increases in the rate of flow, capillary pressure and fluid transudation; (b) compensatory reduction of the vascular bed in areas other than the skin, which allows dilatation in the cutaneous vessels even when the blood volume is unchanged or reduced; (c) increases in blood volume on exposure

to heat which form an alternative method of compensation in lieu of vasoconstriction, and (d) alterations in cardiac output. If these factors could be adequately analyzed, conclusions might be reached which would serve as a guide in the use of heat in physical therapy. Adequate answers are not available at present in many cases, but that need not discourage a statement of the problem.

First, it is well to review the changes in the circulation produced by the employment of relatively intense heat—the acute reactions, which are most familiar. In a peripheral area, such as a limb exposed to heat, dilatation of the vessels occurs so that the blood contained in the area is much greater. Thus Benson¹ finds increases in the volume of the foot and leg immersed in water at from 40 to 47 C. (104 F. to 116.6 F.) which average 2.76 per cent of the volume of the limb. Simultaneous heating of the whole surface of the body should increase the blood content of the skin, probably by half a liter or more. Such a redistribution of blood demands either an increase in blood volume or a compensatory reduction of the vascular bed in other areas.*

The vessels involved in the dilatation are arterioles, capillaries and veins. The great reduction in peripheral resistance which allows rapid rates of flow proves that arterioles are concerned, while the changes in the large veins may be directly observed; changes in the capillaries and venules may be secondary to those in arterioles, but evidence of direct effects is advanced by Capps.² The dilatation is accompanied by a very rapid flow. For instance, Prinzmetal and Wilson³ describe in the normal arm an increase from a blood flow of 1.7 cc. per hundred cubic centimeters per minute in a bath at 24 C. (75.2 F.) to one of 14.9 cc. in a bath at 45 C. (113 F.). The greater part of this increased flow depends on an increased cutaneous circulation, though in such changes the deeper flow to the muscles may also be somewhat increased. The greater rate of flow increases thermal conductivity, allowing rapid transfer of heat inward if the cutaneous temperature is above that of the rectum or of heat outward if the thermal gradient is of normal direction. In either case the increased rate of blood flow makes the surface and deep temperatures approach each other, and it is this fact which makes cutaneous temperature measurements useful in determining the cutaneous circulation.⁴

The vasodilatation in the skin is accompanied by a considerable rise in capillary pressure, as has been demonstrated by Landis,⁵ and this increase in capillary pressure affects fluid transudation, so that edema may accumulate under appropriate conditions at a more rapid rate at the higher temperatures.⁶ In the skin such fluid transudates must increase the moistness of the epidermis and so increase fluid loss by evaporation.

1. Benson, Simon: Volume Changes in Organs Induced by the Local Application of External Heat and Cold and by Diathermy, *Arch. Phys. Therapy* 15: 133-148 (March) 1934.

2. Capps, R. B.: A Method for Measuring Tone and Reflex Constriction of the Capillaries, Venules and Veins of the Human Hand with the Results in Normal and Diseased States, *J. Clin. Investigation* 15: 229-239 (March) 1936.

3. Prinzmetal, Myron, and Wilson, Clifford: The Nature of the Peripheral Resistance in Arterial Hypertension with Special Reference to the Vascular System, *J. Clin. Investigation* 15: 63-83 (Jan.) 1936.

4. Burton, A. C., and Bazett, H. C.: A Study of the Average Temperature of the Tissues, of the Exchanges of Heat and Vasomotor Responses in Man by Means of a Bath Calorimeter, *Am. J. Physiol.* 117: 36-54 (Sept.) 1936.

5. Landis, E. M.: Capillary Pressure and Capillary Permeability, *Physiol. Rev.* 14: 404 (July) 1934.

6. Landis, E. M., and Gibson, J. H., Jr.: The Effects of Temperature and of Tissue Pressure on the Movement of Fluid Through the Human Capillary Wall, *J. Clin. Investigation* 12: 105-125 (Jan.) 1933.

It has been demonstrated⁷ that such adjustments of the degree of moistness of the skin do occur and parallel the changes in circulation through the skin both above and below the true sweating level.

The subject of water loss from the skin is of such importance to physical therapists that it deserves a few moments of digression. This loss may be considered under three heads: (a) water evaporated from fluid transudates of the blood without the intervention of the sweat glands; (b) invisible sweat—invisible since it is evaporated as rapidly as it is secreted—and (c) visible sweat. Loss from fluid transudates can be distinguished from that due to sweat by the fact that there is no loss of chloride with fluid transudates. It is the only method of water loss in the skin in those animals (and the occasional human subjects) which are devoid of sweat glands. In treatment by heat this loss can be entirely prevented if a moist environment is used instead of the relatively dry atmospheres. On the other hand, fluid loss from sweating cannot be prevented; sweating can, however, probably be minimized if the rate of rise of temperatures is kept low. Insensible loss of fluid is largely dependent on the evaporation of transudates; it is by no means a negligible quantity, though much smaller in amount than losses which may be attained with visible sweating. Insensible loss from the skin amounts to some 15 cc. per square meter per hour or more under normal resting conditions and may exceed 50 cc. on exposure to heat. Gross sweating may give losses of the order of 500 cc. per square meter per hour.

The mechanisms involved in local vasodilatation include the local direct effects of heat on the vessels themselves, inhibition of vasomotor tone induced through a rise of temperature occurring centrally in the hypothalamus and inhibition of vasomotor tone induced reflexly. Direct effects of heat on the vessels may be demonstrated in a sympathectomized limb⁸ or in an area completely denervated.⁹ That a rise in central temperature may induce vasodilatation can be seen in the dilatation observable in the vessels of the arm when the feet are immersed in hot water. This does not appear to be reflex in origin, for it occurs only after a considerable delay, and then only when the internal temperature is rising.¹⁰ Such a dilatation is induced through nerve channels and is absent in a sympathectomized limb.

Reflex dilatation due to stimulation of sensations of warmth in the skin has sometimes been denied, though reflex vasoconstriction to cold is generally admitted. Such vasoconstriction may be not only induced but also inhibited reflexly. For instance, exposure of a large area of the skin to quite a small change in temperature gives a sensation of warmth associated with vasodilatation in the skin and a fall of internal temperature through the redistribution of heat.¹¹ Such

changes must have a reflex origin. If the thermal change is great, local effects of heat on the vessels and the mild inflammation which may accompany slightly painful heat may both play a part in the development of vasodilatation. In the inflammatory reactions reflexes of the axon type are probably involved. With changes in surface temperature of 1 degree or less such factors presumably play negligible roles, and true reflexes must be mainly involved.

In response to heat not only is dilatation observable in the skin but there is a compensatory constriction in the central vessels, particularly in the splanchnic area. The reflex character of this response is most readily demonstrated in the central vasodilatation induced on exposure of the skin to cold, for the change then develops very rapidly.¹² Constriction of the central vessels is essential in the adjustment to rapid changes on two grounds: (1) to prevent too great a lowering of the effective peripheral resistance, which would either lower blood pressure or demand a very large cardiac output to maintain the pressure level; (2) to compensate for any increase in the vascular bed in the skin by a reduction in the central vessels. On the balance of these two compensations depends the effect of heat on cardiac output and blood pressure.

Cardiac output may be measured in man, and from its relation to blood pressure the effective peripheral resistance may be calculated. In this way the changes induced by heat can be analyzed. The effect of heat in its early stages is to cause a reduction of the effective resistance to a level some two thirds or one half of the normal; that is to say, the effect of vasodilatation in the skin is only partially balanced by vasoconstriction in deeper areas. The blood pressure is, however, little changed, for the effect of lowered resistance is counteracted by that of an increased cardiac output. It has already been pointed out that the local circulation may be increased by heat to almost ten times the normal; the increase in the rate of flow in the skin's vessels themselves is much greater; the increase in total cardiac output is much less, commonly of the order of from 50 to 100 per cent. Mild heat usually produces a slight fall in blood pressure; with greater heat the increased cardiac output becomes the more important factor and the blood pressure is increased; in either case some constriction of central vessels is probably present. In the early stages this central arteriolar constriction, combined with contraction of blood reservoirs such as the spleen, is able to maintain the vascular bed within normal limits and to insure an adequate venous return to the heart. In later stages reduction of the blood volume through sweating coupled with the continued dilatation of all the vessels in the skin makes the maintenance of an adequate venous return very difficult or impossible. To meet such emergencies, contraction of the central vessels has to be extended, and arteriolar constriction may be employed for its effect on the volume of the vascular bed rather than for that on peripheral resistance. Under such conditions the total effective peripheral resistance may be raised above the normal value in spite of the lowered resistance in cutaneous areas, and the blood pressure may be elevated even though adequate levels of venous return and cardiac output are not successfully maintained. Consequently, a considerable rise of blood pressure on exposure to heat may not be evidence of a good reac-

7. Winslow, C.-E. A.; Herrington, L. P., and Gage, A. P.: Physiological Reactions of the Human Body to Various Atmospheric Humidities, *Am. J. Physiol.* **120**: 288-299 (Oct.) 1937.

8. Freeman, N. E.: The Effect of Temperature on the Rate of Blood Flow in the Normal and in the Sympathectomized Hand, *Am. J. Physiol.* **113**: 384-398 (Oct.) 1935.

9. Trotter, W., and Davies, H. M.: Experimental Studies in the Innervation of the Skin, *J. Physiol.* **38**: 131-246, 1909.

10. Pickering, G. W.: The Vasomotor Regulation of Heat Loss from the Skin in Relation to External Temperature, *Heart* **16**: 115-135 (July) 1932.

11. Gibbon, J. H., Jr., and Landis, E. M.: Vasodilatation in the Lower Extremities in Response to Immersing the Forearms in Warm Water, *Investigation* **11**: 1019-1036 (Sept.) 1932. Uprus, V.; Baths, J. Chin. Investigation **11**: 1019-1036 (Sept.) 1932. Uprus, V.; Gaylor, J. B., and Carmichael, E. A.: Vasodilatation and Vasoconstriction in Response to Warming and Cooling the Body: A Criticism of Methods, *J. Clin. Sc.* **2**: 301-316 (Dec.) 1936.

12. Burton and Bazett.⁴ Uprus, Gaylor and Carmichael.¹⁰

12. Rein, H.: Vasomotorische Regulationen, *Ergebn. d. Physiol.* **22**: 28-72, 1931.

tion; on the contrary, it is apt to indicate that intense arteriolar vasoconstriction has been necessary. In this case it provides a warning that the strain is severe. The vasoconstriction is brought into action, with its consequent reduction in local flow of blood in those areas in which such reduction in flow is least harmful,¹³ but in no area can such vasoconstriction be considered entirely innocuous. Associated with arteriolar constriction there is constriction of large arteries¹⁴ and probably also of veins; reduction of these larger vessels is unlikely to modify to any extent resistance to flow, and it should be considered as exerting mainly a reservoir action. Constriction of all these vessels is not peculiar to incipient circulatory failure from dehydration by heat, for it may be observed in an entirely similar manner, accompanied by the danger signal of a rise in arterial blood pressure in reactions to moderate hemorrhage.

The only alternative adjustment to compensatory vasoconstriction is an increase in blood volume. Evidence of such an increase in the earlier stages of exposure to heat has been advanced by many. There is a slight initial reduction of the hemoglobin, red cell and serum protein concentrations on exposure to warmth.¹⁵ Such lowered concentrations are those to be expected if, through slight vasoconstriction in the splanchnic area, the capillary pressure in the intestinal vessels is reduced and more fluid is absorbed to dilute the blood. Changes of this type are usually temporary, for with acute exposure to heat the water loss is greatly increased and may result in dehydration, so that later the opposite effects of increased hemoglobin, red cell and serum protein concentrations may be seen.¹⁶ Quantitative calculation of the changes in the blood volume is not possible, since the composition of the circulating blood may be modified by the addition of abnormal blood from some reservoir such as the spleen. Up to the present time no valid evidence has been advanced of acute increases in blood volume exceeding 10 per cent of the normal value. In the later stages, when the rate of fluid loss has been much increased through sweating, the blood volume can probably be reduced 10 per cent, 20 per cent or more below the normal volume. According to Kopp and Solomon,¹⁷ reductions in plasma volume of from 10 to 32 per cent are common.

In spite of such a reduction in blood volume, the cardiac output may be maintained through the other adjustments already discussed. However, this is attained only with difficulty, and any relatively slight additional stress may create inefficiency. It is for this reason that the maintenance of an erect posture, with the consequent tendency for blood to accumulate in the dependent lower limbs, may cause inadequate venous return to the heart, decreased cardiac output and fainting, particularly in a warm environment. Failure of

cardiac output, whether produced by a postural change such as that just mentioned or by decrease in blood volume through dehydration, is generated by inadequate venous return. The danger of cardiovascular failure depends on the removal of the normal paths of heat transference; cooling of the body surface is no longer able to lower the temperature of either the heart or the brain appreciably, since blood cooled at the surface is not carried by the circulation all over the body. The most urgent necessity is, therefore, to maintain a normal blood volume and to do this without introducing the opposite hazard of hydremic plethora.

The reactions to moderate heat maintained for a long period differ considerably from those of the acute reaction. Dilatation of the cutaneous vessels is still in evidence, though of a lower order. It is, however, extremely improbable that compensatory vasoconstriction in the splanchnic area can be continued for days. Though some compensation by central vasoconstriction is possibly present, it is probably quite slight, except in the earlier stages, so that the alternative compensation of increased blood volume is utilized. This change is attained slowly, for there must be an increase not only in the salts and water of the blood but also in the total amount of serum protein, which exerts colloidal osmotic pressure and retains the fluid within the blood vessels. In addition, for full efficiency the total amount of red cells has to be increased, a process which takes even longer to reach completion. Though the increase in blood volume is attained slowly, it can be very large.¹⁸ In three male subjects examined in Philadelphia one or more times in both winter and summer, the extreme differences in blood volume have been of the order of from 30 to 40 per cent in each subject, or about 1.5 liters. In all three subjects the smaller blood volumes have been observed in the winter and the larger in the summer. These differences were observed when care was taken to obtain the measurements during maintained cool weather in the winter and during maintained hot weather in the summer; the data therefore do not represent either summer or winter averages, nor probably the maximal changes obtainable under extreme conditions. It is indeed surprising that the changes were as great as those observed, since the subjects were all working in laboratories and in the winter spent most of their time indoors at temperatures of from 21 to 26 C. (70 to 80 F.).

In the earlier stages of warm weather, blood pressures may be slightly reduced and cardiac output is probably slightly increased if the subject is lying down. If the subject is standing, the superficial dilatation of cutaneous vessels favors pooling of the blood in the lower limbs, so that the reduction of cardiac output normally seen on standing is likely to be exaggerated and the difference in pulse rate between the lying and standing positions is likely to be large. Standing becomes a strain, and slight edema of the feet and ankles may be seen. Light work that involves standing may be performed very inefficiently. As the subject adapts to the warm temperatures, these disabilities disappear. Blood pressures become normal or supernormal; standing can be maintained not only with a normal but more commonly with a subnormal reduction in cardiac output and with a subnormal increase in pulse rate. Light work can again be performed efficiently. Probably a large factor in the attainment of such cardiac

13. Rein, H., and Rössler, R.: Die Abhängigkeit der vasomotorischen Blutdruckregulation bei akuten Blutverlusten von den thermoregulatorischen Blutverschiebungen in Gesamtkreislaufe, *Ztschr. f. Biol.* 59: 237-248, 1929.

14. Schretzenmayr, A.: Die Rolle der mittleren und grossen Arterien bei der Regulierung des Kreislaufs, *Klin. Wchnschr.* 15: 625-629, May 2, 670-674 (May 9) 1936. Bazett, H. C.; Scott, J. C.; Maxfield, M. E., and Blithe, M. D.: The Effects of Baths at Different Temperatures on Oxygen Exchange and on the Circulation, *Am. J. Physiol.* 119: 93-110 (May) 1937.

15. Barbour, H. G.; Dawson, M. H., and Newwirth, I.: Water, Salt and Lipid Accumulation in the Serum as a Preliminary to Sweating, *Am. J. Physiol.* 74: 204-223 (Sept.) 1925.

16. Bazett, H. C.: Studies on the Effects of Baths on Man, *Am. J. Physiol.* 70: 412-429 (Oct.) 1924. Barbour, Dawson and Newwirth.

17. Kopp, Israel, and Solomon, H. C.: Shock Syndrome in Therapeutic Hyperpyrexia, *Arch. Int. Med.* 60: 597-622 (Oct.) 1937.

18. Sunderman, F. W.; Scott, J. C., and Bazett, H. C.: Temperature Effects on Serum Volume, *Am. J. Physiol.* 118: 192 (June) 1938.

vascular adjustments is an increase in blood volume, so that any blood pooled in the legs during standing represents a smaller percentage of the total volume.

In order to test the rapidity with which these changes develop, experiments are in progress in which the subjects are maintained in an air-conditioned room under constant conditions differing from those normal to the season. These experiments are being carried on with the cooperation of Drs. J. C. Scott and F. W. Sunderman.¹⁹ A General Electric air-conditioning unit is being used. An experiment of this type requires a great deal of time and the data are as yet comparatively meager. In an experiment started December 26 and lasting to January 2, two subjects entered the room kept at a "normal" temperature of 23.6 C. (74.5 F.) in the daytime and at 22 C. (71.6 F.) at night. After a day at these levels, the temperatures were raised to 32.5 C. (90 F.) during the daytime and to 31 C. (88 F.) at night. The humidity was maintained at approximately 36 per cent. The blood volume increased 6 per cent in one day, 10 per cent in two days and 25 per cent in five days and showed an ultimate increase of over 1 liter in each subject. Even so, the volumes were still below the summer maxima observed in these subjects. With the relatively acute changes in blood volume so induced there was little change in weight, other than that dependent on the alteration in blood volume; with an increase in blood volume of about 1 liter there was an increase in weight of 1 Kg. Changes in weight may indicate the development of changes in blood volume, but, owing to the numerous other factors that may influence weight, such agreement may be absent.

Not only was there an increase in blood volume but with this increase there also developed a greater stability of cardiovascular adjustments. Thus, in one subject the standing pulse rate was at first much more rapid than under control conditions, and the difference between lying and standing pulse rates was exaggerated. As adaptation developed, the standing pulse rate returned to its normal value and the increase in rate on standing was actually subnormal. In the other subject, who adapted more rapidly, the increase in pulse rate on standing was reduced even after one day's exposure to heat. The diastolic pressure observed when the subjects were lying down tended to rise progressively in both subjects. Entirely similar changes in both lying and standing pulse rates and in diastolic pressure in the lying position were observed in data obtained on one of these subjects and on a third subject in 1933 at different times of the year. The cardiovascular adjustments which developed in subjects after a stay of several days in a hot room resemble closely those found in the summer.

Not only is the capacity of adjusting to standing improved but the capacity to withstand dehydration by heat with less disability is also developed.²⁰ It has been shown by Vernon and Warner²¹ that subjects are able to do light work in rooms at a high temperature with less change in rectal temperature, less change in pulse rate and somewhat less fatigue in the summer than in the winter. Such indications of greater fitness may well depend also on alterations in blood volume.

In view of the fact that the Englishman normally lives at relatively low temperatures, changes in blood volume to allow adjustment to higher temperatures may be particularly necessary in his adjustment to tropical or subtropical conditions. Some evidence that this may be the case is afforded by data on blood volume in English subjects in the tropics obtained by Barcroft and his associates,²² for their data indicate an average increase of 38 per cent in blood volume in subjects traveling from England through the tropics. Incidentally their work, published in 1922, was the first to draw attention to the possible effect of a tropical climate on blood volume.

For full efficiency the total amount of red blood cells must also be increased. In the aforementioned hot room experiment both subjects had begun to increase their red cells at the end of five days, but in neither subject was the increase attained proportional to the increase in blood volume. The hemoglobin percentage was therefore reduced, a change not seen in Barcroft's subjects with longer exposure to heat in the tropics. In the aforementioned experiment evidence was obtained, though indirect and incomplete at the present time, that a temporary cooling of a subject for thirty hours might reverse the blood volume change and return it temporarily to normal, even though the subject returned to warm conditions. With the return to normal blood volume, cardiovascular adaptation to the hot conditions was lost. To obtain the beneficial effects of this mode of adaptation, it would seem essential to have the temperature maintained steadily at a high level.

These observations are reviewed in relation to physiological therapy. In producing acute pyrexia, dehydration must be avoided as far as possible. By the use of humid conditions evaporation from the skin, independent of sweating, may be avoided, saving from 10 to 15 per cent of the total loss. This 10 per cent loss may make all the difference between a critical and a noncritical loss. Loss from sweating cannot be prevented. Deductions²⁷ that shock is more liable to occur in a moist atmosphere are erroneous; they depend on a failure to lower the temperature used in proportion to the higher humidity employed. Electrical methods of heating—whether by short or by long waves, by electric field or by electromagnetic field—are valuable but are not necessarily superior, in fact they may sometimes even be inferior to other methods of heating. For local application of heat electrical methods have many advantages in that they can be applied to localities almost inaccessible to other modes of heating. In addition they may allow some slight preferential heating of certain tissues according to the type of wave used. For the induction of general pyrexia they have no essential advantages; on the contrary, the maintenance of an adequate humidity is rendered somewhat more difficult. Methods employing moist air or a warm water spray may ultimately prove simpler, cheaper and more practicable.

Fluid given by mouth should be 0.2 or 0.3 per cent salt solution. Higher concentrations of salt are not indicated, since such solutions are adequate to replace loss of salt in the sweat. Should vomiting occur, replacement should be by the intravenous route and

19. Bazett, H. C.; Scott, J. C., and Sunderman, F. W.: Cardiovascular Changes in a Hot Room, *Am. J. Physiol.* **118**: 11 (June) 1938. Sunderman, Scott and Bazett.¹⁸

20. Bazett, Scott, Maxfield and Blithe.¹⁴

21. Vernon, H. M., and Warner, C. G.: The Influence of the Humidity of the Air on the Capacity for Work at High Temperatures, *J. Hyg.* **32**: 431-463 (July) 1932.

22. Barcroft, Joseph; Binger, C. A.; Book, A. V.; Doggett, J. H.; Forbes, H. S.; Harrop, G.; Meakins, J. C., and Redfield, A. C.: Observations upon the Effect of High Altitude on the Physiological Processes of the Human Body, Carried Out in the Peruvian Andes, Chiefly at Cerro de Pasco, *Phil. Tr. Roy. Soc. London.* **221B**: 351-480, 1922.

then physiologic solution of sodium chloride with dextrose may be employed. Hypertonic saline solution is contraindicated.

Cardiovascular failure develops through inadequate venous return and is accompanied by restlessness. Since inadequate filling of the cardiovascular bed is the primary cause, a blood volume raised initially above the normal value is of great advantage. This may be attained by exposing the subject to mild heat continuously for a few days in advance of treatment. The gain derived depends on an increase in the total amount of serum protein (normal concentration in an increased volume of plasma) which renders fluid retention in the vessels easier. The larger blood volume allows dilatation of cutaneous vessels with less central vasoconstriction. Intravenous infusion of acacia should also be advantageous. By the previous use of such means to increase blood volume or the employment of acacia at the start of treatment it should be possible to extend treatment to patients at present considered poor risks.

During treatment it is desirable to raise the body temperature with as little increase in brain temperature as possible, except perhaps in dementia paralytica. The common practice of keeping the face cool is therefore warranted, but with any such cooling the temperatures that are applied to the rest of the body must be intensified. For such cooling, or for cooling the whole body in an emergency, applications of lukewarm water under conditions favoring evaporation are indicated rather than of ice, for the latter causes superficial vasoconstriction and prevents the cooling extending to the deeper tissues.²³ For the same reason, fluids given by mouth should be at room temperature and not iced. Iced fluids are probably less readily absorbed. Intravenous infusions should be given at room temperature under conditions of high fever with failing circulation.

The possibility of extending hyperpyrexia treatment to a larger group raises the question of the probable effect of such temperature changes on patients with hypertension. In the two subjects investigated experimentally in a warm room, the changes in blood pressure were not great; none the less, the general effect of the warm room was to cause a rise, not a fall, in pressure. Thus the average systolic and diastolic pressures of the two subjects were as follows: on the first control day, lying 107/64, standing 115/91; during the first two days of warmth, lying 112/62, standing 115/86; during the fourth and fifth days of warmth, lying 107/64, standing 125/86, and during the first day and a half after a return to cool conditions, lying 112/69 and standing 124/87. Adaptation to the warm room caused a rise of pressure on standing; return to cooler conditions did not cause any immediate return to a normal blood pressure level; on the contrary, there was some evidence of a temporary further increase in pressure. A rise of systolic blood pressure of this order (10 mm.) has no great significance except that it is likely that such an increase would be grossly exaggerated in a hypertensive subject and that the change then might be very significant.

23. A recent report by E. B. Ferris Jr., H. A. Blankenhorn, H. W. Robinson and G. E. Cullen (Heat Stroke: Clinical and Chemical Observations on Forty-Four Cases, *J. Clin. Investigation* 17:249-262 [May] 1938) indicates that immersion in iced baths gives more effective cooling than does wetting with moist cloths in the air current of an electric fan. The greater effectiveness may depend on the utilization of a larger proportion of the surface in the cold bath. Observations comparing the relative value of cool water at about 25 C. (77 F.) and of iced water in baths under comparable conditions would be of interest.

Reactions of this sort may be concerned with the demonstrable fact that there is a great exacerbation of symptoms in hypertensive cases both in early summer and in the early fall—at times when there are abrupt changes in the external temperature.²⁴ Whether temperature changes are associated with considerable alterations in blood pressure in such hypertensive subjects cannot be properly tested in the laboratory, for such exposures to heat and cold may possibly be dangerous. On the other hand, preliminary exposure to mild heat would probably reduce the risk of frank hyperpyrexial treatments so that such preliminary exposure to moderate heat would be justified in cases in which it was to be followed by real hyperpyrexia. In this way, with adequate study, advancement might be attained not only in the practice of physical therapy but also in the knowledge of hypertension and its dangerous exacerbations. One must assume tentatively that the difficulties likely to be experienced on cooling after prolonged heating would depend on the initiation of generalized superficial vasoconstriction in the presence of a large blood volume, as well as on the existence of an excess of serum protein and of red cells (a rise in hematocrit is demonstrable in the normal subject) and on a consequent increase in blood viscosity during the return of the blood volume to normal.

Such difficulties might be avoided by bleeding as a prophylactic treatment. It may be that in this way bleeding, as utilized so generally in olden times, obtained some of its popularity, for it was common to bleed according to the season. For instance, in Richard the Second, Shakespeare makes King Richard say "The doctors say this is no month to bleed." On the principles here advanced, bleeding would appear most justifiable in the fall. The older physicians seem to have agreed that it was most beneficial in the spring. In this they followed Hippocrates, who advised (VI aphorism 47) "Such as are benefited by bleeding or purging should be purged or bled in the spring." Bleeding in the fall was, however, also common. Hare²⁵ noted the extreme value of bleeding when a plethoric individual suffered from dyspnea on sudden exposure to cold after a period at a warmer, Southern watering place.

CONCLUSION

It seems probable that significant changes in blood volume may be attained by steady, moderate but maintained rise in environmental temperature, while it is doubtful whether a fluctuating temperature can produce the same response. Changes in blood volume in both the upward and the downward direction are therefore controllable; they are associated with marked changes in cardiovascular reactions, and it should be possible to develop logical use of such changes in treatment.

24. Bazett, H. C.: *M. Rec.* 147:301 (April) 1938.

25. Hare, C. J.: Good Remedies Out of Fashion, *Brit. M. J.* 2:151, 1883.

Smallpox and Royalty.—Smallpox was one of the great scourges of the eighteenth century, though syphilis, typhoid fever, measles, diphtheria and influenza were close seconds. It is said that the mortality ratio from smallpox was 50 per cent, there being 60,000 deaths in one year from that disease. . . . Louis XV of France died of it in 1774, as had Mary, queen of England, in 1694. Most of the court beauties, even the Princess Anne, were so pock marked as to spoil their fair skins.—Hurd-Mead, Kate Campbell: *A History of Women in Medicine*, Haddam, Conn., the Haddam Press, 1938.

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

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SATURDAY, NOVEMBER 12, 1938

NORMAL NUTRITION

Knowledge of nutrition continues to advance so rapidly that few are able to keep sufficiently informed to know even the trends of investigation. This advancement has been chiefly by laboratory workers in biochemistry, physiology or animal husbandry and, to a minor degree, by those primarily interested in medicine. The contributions in periodicals have been so voluminous and have covered so many different phases of the nutritional requirements of vitamin, mineral, protein, carbohydrate and fat that the occasional student is bewildered when he attempts to apply practically any portion of the new information.

In a comprehensive review Boyd¹ emphasizes a fact stated by many other observers, "that the nature of the dietary reflects itself in many ways in the manner of life and in the level of health of the people." Ample investigative work supports his conclusion that "the physique or rate of physical growth is conditioned by the adequacy of the diet; that our innate propensities for growth are greater than our response usually indicates; and that our present standards of normality of growth should be considered as average under imperfect nutritional conditions rather than optimum." Studies by other workers, as well as reports from the Health Division of the League of Nations,² indicate that deficiencies of vitamin D and of calcium are more frequent than are those of any other nutritional elements. Such deficiencies not only may result in a suboptimal physical growth³ but are probably of still greater importance in the etiology of dental caries.⁴ There is also an increasing amount of both clinical and experimental evidence that deficiencies of vitamin B₁ and occasionally

other factors in the population of civilized countries, including the United States, may be more common than have been previously believed.

Simmonds,⁵ in a recent article in *THE JOURNAL*, stated that nutrition may now be considered largely a problem of economics and education. The information that is now known and understood by scientists must be conveyed to the average citizen. The knowledge may be of great service if the masses can learn what is essential in balanced nutrition and come to desire it. Simmonds is probably correct when she suggests that "there is too much of a tendency to discuss nutrition in terms of vitamins, essential amino acids, carotene, thiamin chloride, ascorbic acid, nicotinic acid, dicalcium phosphate, calcium gluconate, units of various vitamins in foods and units of various vitamins needed daily by the individuals." To prevent unnecessary confusion, not only for the average patient but for the physician, the question of balanced nutrition must be discussed in terms of milk, meat, potatoes, carrots, oranges or cod liver oil. Such substances are within the radius of experience and knowledge of the average person. The results of laboratory investigations in the field of normal nutrition must be translated into simple common denominators if they are to reach those by whom they are most needed.

NINE YEARS OF RESEARCH ON DRUG ADDICTION

Studies on Drug Addiction,¹ supplement 138 to *Public Health Reports*, is the report of nine years' work under the auspices of the National Research Council with funds provided by the Rockefeller Foundation. The work represents close cooperation between the Research Council and the United States Public Health Service, under whose guidance the clinical studies that form a part of the volume were conducted. The American Medical Association early joined with the Committee on Drug Addiction of the National Research Council in publishing a small volume, *Indispensable Use of Narcotics*,² which was designed to put before physicians what was then known about the use of narcotics in medical treatment. It was hoped by education to keep this use at the minimum for control of pain and for comfort, as it was known that the careless administration of opium derivatives having liability to addiction is responsible for many of the habits contracted by addicts.

In the past it has always been difficult to study cerebral and other living responses of the nervous

1. Boyd, J. D.: Changing Concepts of Normal Nutrition, *Northwest Med.* 37:71 (March) 1938; read before the North Pacific Pediatric Society, Portland, Ore., June 26, 1937.

2. League of Nations: The Problem of Nutrition, New York, World Peace Foundation, vols. 1, 2, 3 and 4.

3. Stearns, Genevieve; Jeans, P. C., and Vandecar, Verva: Effect of Vitamin D on Linear Growth in Infancy, *J. Pediat.* 9:1 (July) 1936.

4. Boyd, J. D.; Drain, C. L., and Nelson, Martha V.: Dietary Control of Dental Caries, *Am. J. Dis. Child.* 38:721 (Oct.) 1929.
Boyd, J. D.; Drain, C. L., and Stearns, Genevieve: Metabolic Studies of Children with Dental Caries, *J. Biol. Chem.* 103:327 (Dec.) 1933.
McBeath, E. C.: Experiments on Dietary Control of Dental Caries in Children, *J. Dent. Research* 12:723 (Oct.) 1932.

5. Simmonds, Nina: Recent Researches in Nutrition in Relation to Preventive Medicine, *J. A. M. A.* 111:1073 (Sept. 17) 1938. *The Dietary History and Its Value in Dental and Medical Practice*, *Am. J. Digest. Dis. & Nutrition* 4:497 (Oct.) 1937.

1. Small, I. F.; Eddy, N. B.; Mosettig, Erich, and Himmelsbach, C. K.: Studies on Drug Addiction, with Special Reference to Chemical Structure of Opium Derivatives and Allied Synthetic Substances and their Physiological Action, Supplement 138 to *Public Health Reports*, their Physiological Action, Supplement 138 to *Public Health Reports*, Washington, D. C., Government Printing Office, 1938; price, 60 cents.
2. *The Indispensable Use of Narcotics*, by Various Authors, Chicago, American Medical Association; reprinted from *THE JOURNAL*, March 14 to June 6, 1931.

tissue. Recently, however, with the introduction of the encephalograph, a new technic has been provided for studying the living neuro-electrical reaction. At the United States Public Health Service Hospital at Lexington, Ky., a beginning has been made in this study by comparing the effect of some fifteen drugs related to the morphine molecule.

Studies on Drug Addiction describes the results of the research in progress since 1929. It discusses the addiction property of morphine particularly as a question of chemiopharmacologic relationship, since the committee's plan of a contribution to the problem of drug addiction conceives the possibility of separation by chemical modification of useful analgesic action and undesirable liability to addiction. To this end the project is a systematic attempt to ascertain (a) the relationship between chemical structure and pharmacologic action in morphine and its derivatives, (b) whether or not it is possible by chemical modification to dissociate the various pharmacologic actions characteristic of morphine, and (c) whether or not a synthetic substance can be obtained comparable to morphine in its analgesic action. The report contains a tremendous amount of data, since it describes the chemical properties, method of preparation and pharmacologic action of more than 300 compounds, most of which were made for the first time in connection with this work.

In the first section of the report, more than 100 derivatives of morphine are discussed. The conclusions indicate clearly that specific chemical modifications do not affect uniformly, either in direction or in degree, all the pharmacologic actions of an alkaloid of the morphine series. In the second section chemical pharmacologic relationships are discussed for more than 200 synthetic substances built up from phenanthrene, dibenzofuran or carbazol. Some of these, especially in the carbazol series, have exhibited a considerable degree of analgesic action in animals. All of the actively analgesic synthetic substances, however, have developed one or more undesirable side actions. The third section of the report describes the clinical studies which have been made in connection with this work, aimed especially at determining the liability to addiction of selected morphine derivatives. A practicable method of quantitative evaluation of the abstinence phenomena, the sine qua non of addiction, is described. Besides it is shown that different substances, differing in their chemical relationship to morphine, vary to some extent in the character and duration of their dependence satisfaction power in known addicts. Clinical pharmacologic studies on non-addicts are also under way and some of the results obtained are given.

The report has been carefully prepared, it is abundantly illustrated by diagrammatic representations of the chemical relationships involved, and each section is clearly and concisely summarized. Included with the report is a complete list of the previous publications

of the units cooperating in the research. Pharmacologists, physiologists, chemists, physicians and all who are interested in the basal problem of the relation of chemical structure and physiologic action of narcotics must be familiar with this work.

THE SCOPE AND FUTURE OF PHARMACOLOGY

Recent contributions in *THE JOURNAL*¹ have reflected a growing concern in the United States over the status of pharmacology. Worldwide interest was demonstrated in this subject by the large attendance and vigorous discussion at a symposium on the scope and future of pharmacology, sponsored by the sixteenth International Physiology Congress at Zurich. In opening the symposium, Sir Henry Dale of London suggested that pharmacology would profit by following the trends of clinical opinion. Clinical interest has turned, he insisted, from the relief of symptoms to the control of causes; clinicians are more concerned now with etiology than with therapeutics. Pharmacologists might help greatly, according to Sir Henry, by orienting clinicians in the uses of such products as hormones to maintain a proper physiologic balance in the human being. Straub of Munich pointed out that pharmacology would probably always have the task of providing physicians with a rational background for the use of drugs. In this regard Starkenstein of Prague remarked on the diverse knowledge required of the pharmacologist in chemistry, physiology, clinical medicine and other fields. Grabfield of Harvard commented on the report of the special committee of the American Society for Pharmacology and Experimental Therapeutics, which recommended that teachers of pharmacology have professional medical degrees. In explaining how a conversation with Sir Henry Dale had led to the symposium, Heubner of Berlin referred to the wisdom of correlating teaching and research in pharmacology as closely as possible with other medical sciences.

Most of the discussion dealt with the teaching of pharmacology in relation to practical medicine. A broader point of view was developed by Leake from California. Defining the science as the study of the action of chemicals on living things, he suggested that its scope is indicated by its special problems and its future is predictable from the applications made of its findings. The special problems of pharmacology, he said, deal with (1) dose-effect relations, (2) the site of drug action, (3) the mechanism of drug action, (4) drug absorption and detoxification and (5) the relation between physicochemical properties and biologic action. Currently, he pointed out, the factual observations of pharmacology are being applied to the diagnosis and

1. David, N. A.: *The Recent Graduate and Drug Nihilism*, J. A. M. A. **106**: 405 (Feb. 1) 1936. David, N. A., and Emerson, G. A.: *The Present Status of Research and Teaching in Pharmacology*, *ibid.*, **107**: 1599 (Nov. 14) 1936. DeGraff, A. C.; MacNider, W. J. B.; Hayman, J. M., and Edmunds, C. W.: *Symposium on the Teaching of Pharmacology*, J. A. Am. M. Coll. **11**: 65, 70, 77, 83 (March) 1937.

prevention of disease in animals and human beings as well as to treatment, to agriculture (pest control and ripening of fruits), to public health (industrial toxicology and control of quackery) and to sociology (crime detection and control of drug addiction).

As emphasized recently, Professor Leake² maintained that pharmacology has a scope and future much greater than that indicated by its traditional relation to practical medicine. Whatever knowledge is contributed by pharmacology regarding the action of chemicals on living things may be used by the alert and imaginative physician in accordance with his judgment to promote the welfare of his patients. The teaching of medical students in this spirit might do much to improve the resourcefulness and increase the responsibility of physicians with regard to the use of drugs.

Current Comment

MEDICAL SUPPLEMENTS IN THE PRESS

Two county societies have recently collaborated in the publication of medical supplements in their local newspapers. On October 25 the Nassau County Medical Society, Mineola, N. Y., published a health section of forty-eight pages in the *Nassau Daily Review-Star* and on October 30 the Wayne County Medical Society, Detroit, published its second annual medical supplement in the *Detroit Free Press*. Both supplements were profusely illustrated and the editorial content was of a high order. Both were published in tabloid form with original front-page layouts, the Nassau society using an interesting arrangement of photographs and the Wayne County society using an original drawing. Not only were the activities and functions of the local societies and the American Medical Association described in both supplements but a wide variety of interesting articles on all phases of medicine and health were used. Such supplements, properly prepared—as these two were—provide an excellent medium of public education in matters vital to health of the individual.

A SYMPOSIUM ON MENTAL HEALTH

The needs of the mentally sick of American communities cannot apparently be met by continuous expansion of public hospital facilities. The answer to the problem from the point of view of medical requirements and economic feasibility must lie in the development of auxiliary community services and measures of an ameliorative, preventive, educational and social nature. In an effort to bring the scientific, educational and social resources of the nation to bear on a coordinated, fundamental and more effective attack on the whole problem of the cure, control and prevention of mental illness the American Association for the Advancement of Science, through its section on medical sciences, proposes to hold a symposium on mental health

at its winter meeting in Richmond, Va., in December.¹ This symposium will occupy three consecutive days, beginning December 28 and ending December 30. Unlike the usual scientific meeting, the majority of the communications will not be read at the meetings but will be published in advance and used as a basis for discussion, thus freeing the conference period for extensive consideration of the more vital issues. It may well be that problems of mental health are the most serious of all the medical problems which now concern the nation.

MICROSCOPY

Progress in the mechanical development of the microscope has reached such a stage that the inner structure of bacteria, small colloids and many viruses can be readily visualized.¹ The availability of an instrument of such quality will doubtless lead to the determination of the causes of diseases which have heretofore resisted identification. Furthermore it is likely that within a short time further technical developments in microscopy will open up new avenues of research. In addition, fluorescence microscopy has already, at least in an experimental way, gained a foothold in establishing the presence of tubercle bacilli in the tissues.² These developments, which are generally termed pure science, are likely to lead to still greater strides in medical science.

DENTAL CARIES IN SIBLINGS

Recently Klein and Palmer¹ analyzed the dental status of two groups of children, one designated as caries immune and the other as caries susceptible. The study was particularly related to the incidence of caries in siblings. Basic data were obtained from examinations of 4,416 elementary school children who comprised 94 per cent of the entire enrolled grade school population of a small urban community (Hagerstown, Md.). Carious lesions were determined by trained dental officers. By means of certain criteria carefully outlined, 357 of the children were designated as caries immune and 270 as caries susceptible. Two immune siblings were observed in each of twenty-seven families and two susceptible siblings in each of thirteen families; three immune were found in each of two families and three susceptible in three families, and four immune were observed in one family. In each of two families one immune and one susceptible were found. Analysis of the results indicates that siblings of those susceptible to caries have more than twice as much caries in both the permanent and the deciduous teeth as do siblings of the immune. These conclusions were based on a sufficiently large number of cases to constitute statistically valid evidence, and the authors therefore believe that the existence of familial resemblances in carious experience of siblings is definitely established. No specific explanation is offered for the observed familial differences.

1. Soule, M. H.: The American Association for the Advancement of Science, *Science* 88: 302 (Sept. 30) 1938. News Comments, *Mental Hygiene*, October 1938.

1. Das Uebermikroskop, *Chemiker-Zeitung* 62: 561 (Aug.) 1938.

2. Haitinger, M.: Fluoreszenzmikroskopie, *Chemische Novitäten* 1: 1 (July) 1938.

1. Klein, Henry, and Palmer, C. E.: Familial Resemblance in the Caries Experience of Siblings, *Pub. Health Rep.* 53: 1353 (Aug. 5) 1938.

2. Leake, C. D.: *Prolegomenon to Current Pharmacology*, Univ. California Publ., *Pharmacol.* 1: 1 (March) 1938.

ORGANIZATION SECTION

THAT PHILADELPHIA OBSTETRIC CASE

Recently many newspapers have commented on the report of a case in which a woman in Philadelphia gave birth to a child prematurely without medical assistance at the time of birth. Apparently a police report on the case said:

Woman was out of funds; hence unattended delivery. Nothing suspicious.

The Philadelphia *Record* says this indicates

Plenty of grounds for suspicion concerning the medical profession's responsibility and adherence to its own rules of ethics, about which the public hears so much.

According to the newspapers, a policeman called six physicians in the neighborhood and all refused to leave their homes at 7 a. m. on a charity case. The baby, it appears, was born dead. This case was made the basis of a column by the Philadelphia *Record's* columnist, Mr. Jay Franklin, who has not neglected a single opportunity in recent months to assail the medical profession and to exalt collective medicine.

He concludes his column with the statement:

I think it is up to Dr. Fishbein to make a swift investigation of the facts as to this incident in Philadelphia and to make those facts public.

Mr. Westbrook Pegler in his column says:

Not to find fault too readily with the press work on the story of the destitute Philadelphia woman, I suggest, nevertheless, that the account left untold facts which were no less important than those it did tell. How came the patient not to have made arrangements for attendance in an expected emergency? Was it any fault of hers or the husband's, or can it be that Philadelphia simply does not give such assistance? If free care is available is it, then, the duty of the doctors and social service workers to go about scouting for patients? And, finally, what about the six doctors? What were their reasons, and did any one even trouble to ascertain whether they were already occupied with more forehanded patients or, perhaps, thought it was a case which the ambulance service should take in its stride?

THE FACTS IN THE CASE

Here are the facts in the Philadelphia incident as reported to THE JOURNAL: On Sunday morning, October 23, at 7 a. m., the patient was delivered of a six or seven months stillbirth at a rooming house to which she went only about an hour before. Her home address is not known, and she was in labor on arrival at the rooming house. She had previously been taken to two hospitals by a roomer and had been examined and refused admission at both hospitals because of not being registered in either as a patient. She was then returned to the rooming house. One of the roomers called the sergeant at the police station, who failed to call the district physician because he said he did not wish to disturb him on Sunday. The roomer then tried to reach five different doctors in the neighborhood. The first doctor was taking a bath at the time when his doorbell rang, and when he answered the doorbell no one was there. He reported that he had not taken care of an obstetrics case for thirty years. The second doctor, who was a specialist in diseases of the eye, was asleep and did not answer the doorbell. The third doctor who

was called does not practice obstetrics, but he offered to send an ambulance for the patient. This offer was refused. The sergeant at the police station telephoned to a hospital and the assistant chief resident offered to call on the woman if the police would send a car. On his arrival at the rooming house, the resident found the patient and the dead infant, which had delivered spontaneously. He administered treatment to the mother and left with instructions to call the hospital if further treatment was necessary. This patient refused to answer any questions, made no statements and disappeared one week later. It appears that there are ten hospitals within a distance of from three blocks to one and one-half miles from the place in which this delivery occurred. For some reason it is now impossible to secure statements at the rooming house concerning the incident.

A CASE IN CHICAGO

Physicians know that such incidents occur in all large cities and there seems to be considerable doubt as to whether the condition could be improved under any other system of medical care than that which now prevails. In Chicago during the month of October 1936 the following incident occurred: A Negro girl aged 17, not married, gave birth to a child prematurely at the seventh month in a rooming house which was within a mile and a half of seven hospitals. The coroner's examination indicated that the child had died of exposure following birth. In this instance the patient stated that her progress had been normal throughout her pregnancy. A week before the birth of the child she had visited a Negro hospital in the vicinity and was advised to return within a few days for additional treatment. The child was born spontaneously. A caretaker in the rooming house, finding the child born, called the Negro hospital and was informed that it was impossible to send a physician and that the patient should call the Cook County Hospital. She called the Cook County Hospital and was told that it was impossible for them to take care of the patient because she had been registered in the Negro hospital. At the Cook County Hospital she was told to call the police station. She called the central police station, which transferred the call to the Wabash Avenue station, which informed the woman that it was impossible to give attention since the baby was already born. A call made to an emergency relief agency resulted in a statement to the effect that it would be desirable first to file a regular application. Obviously in this instance several public agencies failed simply because of ignorance of those answering telephones of the fact that the Chicago Maternity Center, the Chicago Lying-In Hospital and other agencies within the vicinity could have provided service on request. Incidentally, in this case the first physician who was called on the telephone responded immediately but unfortunately arrived after the birth of the child.

NO PROTECTION AGAINST IGNORANCE

A study of the facts in the Philadelphia case will reveal to any one that the physicians of the community were certainly not at fault. There can be no protection

against ignorance. Neither can there be protection against the unwillingness of the public to cooperate with available agencies whether governmental or private. Mr. Franklin and the *Philadelphia Record* have

again done serious harm to the reputé of the medical profession by publishing an attack without adequate investigation. The least that they can do now is to publish the facts.

AMERICAN MEDICAL ASSOCIATION STUDY OF MEDICAL CARE

The Washington County (Iowa) Medical Society analyzed and compiled the facts developed in the Study of Need and Supply of Medical Care for that county and drew the conclusions from the facts so thoroughly that the society's summary is published as received.

Washington County, Iowa

Washington County, situated in the southeastern part of Iowa, has an area of 576 square miles and a population of approximately 20,000. The county seat, located near the center of the county, has a population a little short of 5,000. There are eight other towns in the county, besides several villages. Physicians are located in seven of the towns, there being nineteen physicians in the county in active practice, seventeen in general practice and two in special practice.

Washington County is essentially a farming community, three fourths of the population living on farms or in cities under 1,000. There are, however, several industries. The Maple Crest Hatcheries at Wellman employ, during the season, from 150 to 250 persons. Brighton has a canning factory which employs a number of people during the harvest season. In Washington the American Pearl Button factory employs about 150 persons, the McCleery Calendar factory from fifteen to thirty-five, the Continental Telephone Company from twenty-five to thirty, the Iowa Southern Utilities Company from twenty-five to forty and the Washington school system employs about sixty-five teachers and town and rural schools employ another 160.

Washington County was settled to a large extent by people from Ohio, Pennsylvania and Illinois. There are Bohemians, Swedes, Norwegians, Hollanders and people of Welsh extraction but comparatively few foreign born people in the county. The Negro population of Washington County amounts to less than 0.25 per cent of the population.

As to the economic conditions in Washington County, it is said that approximately 75 to 80 per cent of some 2,500 farms in the county are farmed by tenants. A considerable number of these are sons or sons-in-law of the owners. In addition, according to the Farm Security Administration, seventy-eight rural rehabilitation loans have been made during the last three years in this county.

The Relief Office states that there are eighty-eight families on WPA, fifty families (283 individuals) receiving direct relief from the FERA and approximately eighty-two families and twenty-nine single persons (aggregating 346 individuals) receiving relief from the county. It is estimated that these families will aggregate approximately 800 individuals. In addition, there are between 375 and 400 persons receiving old age pensions.

THE CARE OF THE INDIGENT

For several years the Washington County Medical Society has had an exclusive contract with the board of supervisors for the medical care of the indigent of Washington County. The laws of Iowa require that

this arrangement provide full medical care. Therefore quasimedical sects may not participate in such an arrangement.

During the winter of 1930 a member of the Washington County Medical Society suggested to the Medical Economics Committee of the Iowa State Medical Society that a standard fee bill be prepared which could be used as a basis for negotiations for county medical societies throughout the state. This was done and the standard fee bill was adopted by the house of delegates of the Iowa State Medical Society in May 1931. This fee bill has since been used extensively for the purposes for which it was intended.

The contract which the Washington County Medical Society has had with the board of supervisors provides that bills shall be submitted monthly after having been sanctioned by the welfare officer, based on this accepted fee bill, and payment shall be made to the society at a percentage fee of this contract. In this county this amounts to about 54 per cent. The money is prorated to the members of the society in the same proportion that the total of his bills bears to the amount of money on hand, after dues to the state society for each member and the expenses of the society for meetings and other projects during the year have been paid. This work takes about 6 per cent of the total amount of money received. The members therefore receive in cash approximately 50 per cent of the fees of the bills.

By arrangement with the board of supervisors and the relief office, the annual quota to the University Hospital being fifty-three, an effort is made to fill this quota with patients who cannot readily be taken care of in the local county hospital—that is, persons with disease of the prostate, rectal cancer, some complicated fractures, and so on. The board of supervisors has directed the relief office not to send any patient to Iowa City who can be efficiently cared for at home, unless it is done at the doctor's request.

In addition to this contract for medical care the society has a supplementary contract for the care of surgical patients. This is based on 30 per cent of the standard fee bill, or \$40.50 for a major operation. This includes all care of the patient while in the hospital. This arrangement has been extremely satisfactory over a period of years to the medical society members, to the board of supervisors, to the welfare worker and to the people concerned. During the year 1937 the society was paid, for surgery, the sum of \$1,308 and for general medical care—which includes obstetrics, fractures and minor surgery—the sum of \$3,286.69.

WELFARE AND RELIEF AGENCIES

Under authority of the statutes of Iowa the Board of Supervisors has, for several years past, maintained a relief office under the charge of a competent investigator. It is the duty of this officer to investigate the financial standing of all persons who desire commitment to the state hospital or to patients who desire medical or hospital care within the county. The law provides that, if patients committed to the state hospital, exclu-

VENEREAL DISEASE CONTROL

For the past two years the director of the health unit has taken an active part in education concerning the incidence and treatment of venereal diseases and, as a part of his work, has done some treatment to properly certified patients. It is the plan of the Washington Medical Society, as directing the county health unit, to provide for the establishment of a demonstration unit in this county for the purpose of establishing and maintaining adequate measures for the prevention, treatment and control of syphilis. This plan implies education concerning the incidence of syphilis and possibility of its control and the necessity of permitting tests to be made and securing proper treatment when the disease is present. Plans for this project are now in the making and a copy will be filed with this report at an early date.

PREVENTIVE MEDICINE

Following the meeting of the American Medical Association in Chicago in 1924, toxin antitoxin was obtained from Abraham Zingher from the New York City Board of Health and was administered to pupil nurses and others in Washington during July of that year. This appears to have been the first toxin antitoxin which was used in this part of the country. The Washington County Health Unit was first organized in the same year and through all the ups and downs the health officer has continued educational campaigns looking toward immunization of school children against diphtheria and smallpox. Every year some immunization has been done and the school boards in two or three of the smaller towns have paid the local physician a lump sum to immunize all the children. Four or five years ago in Crawfordsville, 198 children of 200 were immunized. All together a goodly percentage of the children who are now in high school have been immunized. There remains a considerable amount of work to be done among younger children. However, not one case of diphtheria has originated in Washington County for ten years. During that period three cases have been brought in from the outside.

The members of the Washington County Medical Society have, for a number of years, been quite active in preschool examinations, in summer roundups and in 4-H Club examinations. Each year prior to the state fair a large number of boys and girls are examined in order to find the best one of either sex to send to the state fair. As the health unit appears to be more firmly established than ever before, we look forward to a much greater number of children to be immunized as time goes on. The value of health work in 4-H Club examinations cannot be easily estimated, but it is recognized by the local county medical societies that it is an important part of their work, and work is cheerfully and willingly done.

Typhoid fever is practically unknown in Washington County. A few cases of undulant fever have been found during the past few years.

COUNTY TUBERCULOSIS ASSOCIATION

In 1936 a member of the society was asked to head the work of selling Christmas seals in the county. The work was accepted on two conditions: that (1) the organization should be county-wide and all money collected should go through one office, and (2) the doctor mentioned should select the executive committee. This was acceded to. During the winter of 1936 the groundwork was laid in preparing an effective organization which would be able to function the full year. The

definite plan was that the large percentage of the money should be used for the good of the people of Washington County and all of it for tuberculosis work. None of this work has ever been done before. Through the cooperation of the school teachers of the county and the parent-teachers association in Washington a good start was made. Through the work of this same physician the state tuberculosis association arranged to cooperate with the state board of health to employ a full-time physician and nurse assistants for tuberculosis work, and, further, if the local Christmas Seal committee put into the health unit a sum of money equal to \$10 per thousand of the county population the state tuberculosis association would put the same amount to the credit of the state board of health. In counties having no health organization the \$10 per thousand was to be sent to the state board of health. Then the state board of health would double this amount in money and services for work in the county.

In carrying out this plan a chest clinic was held in the Washington County Hospital July 15, 1937, at which time 103 patients were roentgenographed, these patients being persons who either had active tuberculosis or had been associated with persons who had active tuberculosis within the past five years. A second similar clinic was held Nov. 16, 1937, at which time eighty-seven roentgenograms were taken, and on July 15, 1938, a third chest clinic was held and 132 chest roentgenograms were taken. The plans of this association for the winter of 1938 are rapidly nearing completion. The same plan of education will be continued.

MATERNAL DEMONSTRATION UNIT

Beginning July 1, 1936, there was organized, under the supervision of the Washington County Medical Society, a maternal demonstration unit, to work in close harmony with the health unit. The two nurses, devoting full time to this, were Miss Nadeau and Miss Brouillette. The duties of these nurses were to visit all expectant mothers, with the consent of the attending physician, to give such advice and render such assistance as might be needed, to explain to the woman the necessity of medical supervision, and to urge that it be procured; also to assist the doctor at the time of delivery for those persons who are unable to provide nursing service.

The usefulness of this unit has steadily grown and on July 1, 1937, it was placed directly under the health unit; both units were supervised by a committee of the county medical society. The nurses in charge at present are Miss Pearl Olsen and Miss Aila Hiltunen. During the past year stress has been placed on the necessity of blood examination for syphilis. A very large percentage of blood examinations are now being made. In 1937 there were 335 babies born in the county, 111 of these in the Washington Hospital. Sixty-eight deliveries at home were attended by maternal demonstration nurses, and at fifty-one others other registered nurses were in attendance; that is, registered nurses were in attendance at 70 per cent of the deliveries, either in the hospital or at home, and practical nurses were in attendance at forty-five others. Thus, in 80 per cent plus of all deliveries advance preparations were made for assistance. This unit provides sterile packets containing basins, soap, gloves, gowns, sheets, towels, gauze and cotton, thus insuring that every delivery will be effected under septic conditions. Last year 316 of these packets were prepared. Doctors living near the

edges of the county are permitted to use them in their practice outside the county and if a packet is not used within sixty days it is resterilized. This accounts for there being more packets used than there were deliveries in the county.

In 1937 53 per cent of the expectant mothers consulted their doctor before the fourth month. In the first six months during the year 1938 this figure had reached 60 per cent. In 1937 69 per cent had consulted the doctor before the end of the sixth month. During the first six months of 1938 this had risen to 79 per cent. Not a single mother died in the county during 1937 from causes connected with childbirth.

HEALTH UNIT

The health unit was first organized in Washington County in 1924 with financial assistance from the Rockefeller Foundation. This unit has continued to date except for two or three interruptions due in the main to political reasons. The unit was reestablished early in 1936 and began operations July 1 of that year—now organized under provisions of the Social Security Act of 1935, whereby sums of money listed for health work in the county are doubled by funds from the Public Health Service.

This unit requires a medical director with public health training, a sanitary engineer and two nurses, one of whom confines her activities to the city of Washington. Dr. R. M. Sorenson was the first medical director, R. J. Schliekleman the engineer, Miss Laura Einspahr city nurse, and Miss Stella Jorpeland county nurse. The duties of the engineer include investigation of the water and sewerage supplies of all schools and public buildings in the county, advice concerning lighting, heating and seating of schoolhouses, advice to town councils relative to water and sewerage problems, and administration of milk ordinance in Washington. The duties of the nurses are visiting various schools, inspection of children, home visits where indicated, and educational procedures. The medical director's main duty is education in health problems, including the use of preventive measures against communicable diseases, oversight of quarantine, and general assistance to all the doctors in health problems. The influence and activity of this health unit have continued to grow. The present director is Dr. D. C. Barrett and the county nurse is Miss Luther. The city nurse is Miss Jeffrey. The engineer remains the same.

There are 104 county schools, two parochial schools and eight public schools outside Washington. In Washington there are six public schools and one parochial school—all of which receive health services and supervision as needed. The birth rate in the county in 1937 was 16 per thousand. The death rate was 11 per thousand. The infant mortality rate was 44 per thousand. There was not a maternal death due to childbirth during the year. There has not been a case of diphtheria originating in this county for ten years; three patients have come into the county after having contracted diphtheria during that period.

SYPHILIS

Plans have been made locally and submitted to the United States Public Health Service for approval to establish and maintain adequate measures for the prevention, treatment and control of venereal disease, as proposed in the Act of Congress S. 3290, an amendment to the Act of July 9, 1918, after section 4,

chapter 15 (40 Stat. 886; U. S. C., Title 42, Section 25). The plan submitted provides for reasonable payment to members of the Washington County Medical Society for the treatment of syphilis; it provides that the director of the health unit may take specimens of blood from groups who voluntarily request such action, and that the doctors may be paid a reasonable fee for the taking of blood specimens of those requesting it and the specimens to be submitted to the laboratory of the Washington County Hospital for examination by the Kline test. Those specimens which are found to be 3 plus or 4 plus by the Kline test will be submitted to the state hygienic laboratory for further examination by the Wassermann or Kahn test. The director of the health unit will receive no fee for any work he does in caring for the foregoing.

Those persons found with positive evidence of syphilis will be referred to their family physician and if found to be county charges the doctor will be paid as already noted. The remedies to be used will be furnished by the state board of health. The plan suggests that the expense of the hospital, that is, glassware and antigen, be provided by the United States Public Health Service and that a small monthly stipend be paid so that the hospital may employ a maid to do some of the detail work and relieve the nurse technician from these duties. The Phalanx Club, an organization of young men in Washington, is encouraged to begin publicity for blood tests as soon as we receive approval from the Public Health Service. It is estimated that the sum of \$1,000 will carry this plan forward to the end of this fiscal year, that is, June 30, 1939, payment to be made on the filing by the doctor of proper records and to be prorated according to the same plan as is in operation with the society contract.

SUMMARY

In the survey of the need for medical care in Washington County and the facilities available we draw these conclusions:

There are in active practice in the county nineteen well qualified physicians; two of them are in special practice, leaving seventeen for general practice. It is found that no person in the county is more than 8 miles from a physician, and it is possible for a physician to reach any patient within fifteen or twenty minutes, except for a few weeks in the spring when the dirt roads are almost impassable. Still, it is possible for a physician, in any condition of the roads, to get [with automobile or other conveyance] within 2 or 3 miles of any home. The very efficient work of the Washington County Medical Society assures competent physicians.

There are twelve nurses in the county for general duty—eight of them for full-time and four for part-time duty. The hospital organization and equipment are available to all residents of the county. There are 119 schools which are well supervised by the health unit. There are twelve pharmacists in the county, who cooperate quite well in matters medical. They do not, when asked to refer some one to a physician, insist on selling a "patent medicine." In fact, we have reason to believe that the sale of "patent medicines" in this community had decreased markedly in the past twenty-five years.

There are twelve dentists in the county who assure us that they do not refuse remedial dental work even if the patient is unable to pay. They do insist on pay for corrective dental work. We are told that not

25 per cent of the people avail themselves of the work of the dental profession and that 50 per cent of the school children need dental work. This is not the fault of the dental profession but it does show that the community needs much education as to the availability of dental services and as to the necessity of securing such services when needed. The county medical society furnishes adequate medical and surgical attention to the low income group, regardless of their ability to pay. The society members receive reasonable recompense for the care of the indigent. The educational work carried forward and the maternal demonstration unit are producing increasingly gratifying results.

Under direction of the society there has been conducted yearly for five or six years educational campaigns to have children protected against diphtheria and smallpox. This effort has attained considerable success, but still the percentage of protected children is too low. The next step in the near future is to attempt to immunize children between the ages of 9 and 24 months. The local Red Cross chapter has contributed \$100 for this work.

The records show that the physicians of this county during the year of 1937 cared for in their offices or homes between 1,500 and 2,000 patients from whom no payment is expected.

The close cooperation of all the agencies interested in public health in the county—that is, the county medical society, the hospital, the health unit, the maternity unit, the tuberculosis association, the board of supervisors, the welfare officer and other interested groups, such as schools, Rotary Club, chamber of commerce, Farm Bureau and Red Cross—is necessary for the successful planning for public health, and as this procedure has been functioning for a sufficient length of time to demonstrate that the plan is good and that good results are now being accumulated there is no working at cross purposes by the agencies named or by groups in Washington County.

More and more people are learning to appreciate the medical services which may be given them. There are, of course, in the community a certain percentage of people who prefer the services of quasimedical practitioners and do not avail themselves of medical services. That is their privilege.

Reviewing all the facts as presented by this survey, the medical profession of Washington County feels assured that the medical services are adequate, that their acceptance is quite general, and that there is no necessity for any change in the application of the medical services available to the needs of Washington County.

OFFICIAL NOTES

HEARINGS BEFORE THE GRAND JURY IN WASHINGTON

In addition to the witnesses mentioned in recent issues of THE JOURNAL, the newspapers report the following persons as having testified last week before the Special Grand Jury in Washington, D. C.: Dr. Raymond E. Selders, medical director of the Group Health Association, Inc.; Dr. Richard H. Price of the staff of the Group Health Association; Drs. Allan E. Lee and Richard Stephen Hulburt, both of whom are said to have resigned from the staff of the Group Health Association several months ago; Rev. David D. McCauley, dean of Georgetown University Medical School; Drs. George B. Tribble and Roy D. Adams, both of Washington, D. C., and Mr. and Mrs. William A. Anderson, who joined the Group Health Association, Inc.

SECTION REPRESENTATIVES TO THE SCIENTIFIC EXHIBIT

The following physicians have been appointed by the different sections of the Scientific Assembly as representatives to the Scientific Exhibit for the St. Louis session, May 15-19:

- Practice of Medicine—Fred M. Smith, University Hospitals, Iowa City.
- Surgery, General and Abdominal—Grover C. Penberthy, 1553 Woodward Avenue, Detroit.
- Obstetrics and Gynecology—H. Close Hesseltine, 5841 Maryland Avenue, Chicago.
- Ophthalmology—Georgiana Dvorak-Theobald, 720 Medical Arts Building, Oak Park, Ill.
- Laryngology, Otology and Rhinology—Lee Wallace Dean Jr., Barnes Hospital, St. Louis.
- Pediatrics—Arthur F. Abt, 104 South Michigan Avenue, Chicago.
- Pharmacology and Therapeutics—Wallace M. Yater, Georgetown University Hospital, Washington, D. C.
- Pathology and Physiology—F. W. Konzelmann, Temple University Hospital, Philadelphia.
- Nervous and Mental Diseases—Roland P. Mackay, 8 South Michigan Avenue, Chicago.

Dermatology and Syphilology—Hamilton Montgomery, 102 Second Avenue S.W., Rochester, Minn.

Preventive and Industrial Medicine and Public Health—Paul A. Davis, 1436 Delia Avenue, Akron, Ohio.

Urology—R. S. Ferguson, 121 East Sixtieth Street, New York.

Orthopedic Surgery—F. A. Jostes, 3720 Washington Boulevard, St. Louis.

Gastro-Enterology and Proctology—Sara M. Jordan, 605 Commonwealth Avenue, Boston.

Radiology—Elwood E. Downs, 509 North Broad Street, Woodbury, N. J.

Application blanks for space may be obtained from the Section Representatives or from the Director, Scientific Exhibit, American Medical Association, 535 North Dearborn Street, Chicago.

RADIO BROADCASTS

The fourth series of programs broadcast in dramatic form portraying fictitious but typical incidents of significance in relation to health by the American Medical Association and the National Broadcasting Company, entitled "Your Health," began Wednesday October 19 and will run consecutively for thirty-six weeks. The program is broadcast over the Blue network of the National Broadcasting Company each Wednesday at 2 p. m. eastern standard time (1 p. m. central standard time, 12 noon mountain time, 11 a. m. Pacific time).¹

These programs are broadcast on what is known in radio as a sustaining basis; that is, the time is furnished gratis by the radio network and local stations and no revenue is derived from the programs. Therefore, local stations may or may not take the program, at their discretion, except those stations which are owned and operated by the National Broadcasting Company.

The next three programs to be broadcast, together with their dates and their topics, are as follows:

- November 16. Healthful Play.
- November 23. Weather and Wearing Apparel.
- November 30. Rest, Relaxation and Recreation.

1. Owing to program conflicts, there will be no Chicago broadcast of the network program. Instead, a recording of the program will be broadcast over Station WENR at 8 p. m. each Wednesday. This recording will be an identical rebroadcast of the network program broadcast earlier the same day.

WOMAN'S AUXILIARY

Illinois

The auxiliary to the Chicago Medical Society held its first general meeting of the autumn at the Chicago Woman's Club, October 5. The speakers were Dr. Robert H. Hayes, president, and Dr. Frank F. Maple, secretary of the Chicago Medical Society. Dr. Hayes spoke on "What Have We to Look Forward to in the Practice of Medicine?" and Dr. Maple on "The Value of the Auxiliary."

Missouri

The Cass County Medical Society and the auxiliary held a joint meeting at Belton recently. Dr. Ralph R. Coffey of Kansas City was speaker.

Fifty-seven members of the auxiliary attended the annual board meeting at Columbia September 20. The subject of the essay contest, "Highway Hazards," was chosen at this time. The members will attempt to make the essay contest in the public schools a state project.

The program for the Missouri auxiliary for 1938-1939, prepared by Mrs. A. H. Horne, chairman of the program committee, will have as topic for the year "The House of Medicine."

The twenty-sixth district auxiliary held its annual picnic for the doctors and their families at Arlington in August with forty people attending.

Utah

The auxiliary to the Utah State Medical Association held its annual meeting at Ogden September 1-3; more than 100 members attended. Dr. E. N. Neher, chairman of the advisory council of the auxiliary, was speaker at the board meeting September 1. At the opening meeting Dr. M. J. Macfarlane, president of the Utah State Medical Association, was the speaker.

At the luncheon meeting Mrs. J. W. Aird of Provo spoke on the "Doctor's Wife as a Legislator." The program of the general session was a round table discussion led by the Utah members of the board of directors of the Auxiliary to the American Medical Association, Mrs. L. S. Merrill, Mrs. L. J. Paul and Mrs. Henry Raile.

At a dinner with Mrs. W. M. Stookey presiding, socialized medicine was discussed by Dr. John Z. Brown and Mr. W. H. Tibbals. Dr. Milton J. Rosenau spoke on "Fads and Fancies of Preventive Medicine and Public Health" at an open meeting September 1.

At the general session, September 2, Dr. Alma Nemir spoke on "The Preparation of Teachers for the School Health Program" and Judge Reva Beck Bosone spoke on "Petty Crimes and Traffic Offenses."

Dr. Irvin Abell, President of the American Medical Association, spoke at the breakfast given by the auxiliary at the Ogden Country Club September 3. Mrs. C. L. Schields, president of the Utah Auxiliary, 1937-1938, and Mrs. W. M. Stookey, president for 1938-1939, presided at these meetings.

West Virginia

Reorganization of the Raleigh County auxiliary in southern West Virginia, with an active membership of thirty-five, makes a total of twelve auxiliaries in the state.

An essay contest on "How to Prevent Contagion" will be sponsored in the Fairmont schools by the Marion County Auxiliary.

Fayette County recently placed Dr. William F. Snow of New York on the program at New River College auditorium for a talk on "Syphilis."

A five dollar prize has been offered to the county having the largest increase in *Hygeia* subscriptions. Logan County has placed thirty-one in the schools; Cabell and Raleigh counties have pledged forty and thirty subscriptions respectively.

A special research project for the year is the compiling of the biographies of the past presidents of the state medical association from 1867 to 1938.

Mrs. C. C. Tomlinson of Omaha, National Auxiliary president, was honor guest and speaker at the meeting of the state executive board in Charleston October 11. This meeting was presided over by Mrs. Frank S. Harkleroad of Beckley, state auxiliary president. Sixty auxiliary members from all organized counties in the state were present at the luncheon.

MEDICAL ECONOMIC ABSTRACTS

POSSIBLE PROGRAM OF SICKNESS
INSURANCE

A suggestion as to changes that may be proposed in social security legislation is contained in a discussion of "Three Years' Progress Toward Social Security" by Arthur J. Altmeyer, chairman of the Social Security Board, in the *Social Security Bulletin* (1:6 [Aug.] 1938), in which he says:

"One respect in which our social insurance system is not yet as complete as those of many European countries is in its failure to provide compensation for loss of income because of illness or disability. The Social Security Act attempts to prevent or alleviate some of the distress caused by illness through federal grants to the states which enable them to strengthen their public health services, to extend care for crippled children, and to provide for maternal and child health and for vocational rehabilitation of the physically disabled. Compensation for the enormous wage loss due to illness and disability would seem to be our most important next step toward security of income. The recent National Health Conference was invaluable as a means of clarifying many of the complex problems involved in establishing an adequate nationwide program of health protection and in suggesting alternative lines along which solutions may be sought.

"It would seem that compensation for periods of temporary illness might well be coordinated administratively, when it comes, with our existing insurance provisions. If, as seems likely, it develops as a federal-state program, the taxes necessary to finance the system might well be collected at the same

time as unemployment insurance contributions and by the same agency. Payment of disability benefits, however, presents a distinct problem. For while unemployment compensation benefits are paid to workers who are unemployed but able bodied and available for work, disability benefits are paid to workers who are unemployed under exactly opposite circumstances, that is, because of inability to work. With workmen's compensation already in operation for a number of years in practically all states, it may be desirable to take advantage of the experience of these agencies in administering the new but closely related disability insurance payments. These problems must be explored at length and with regard for the corresponding need to expand social insurance or other methods of providing security against the costs of sickness care."

MEDICAL CARE PLAN ABANDONED
IN WASHINGTON

We have been informed through a communication from Dr. Clarence A. Smith, editor of *Northwest Medicine*, that the plan described in the October 15 issue of *THE JOURNAL*, page 1475, on "Care for Social Security Clients in the State of Washington," "was abandoned in the spring of 1938 due to suspension of federal contributions and lack of state funds." Because of this lack of funds, care of the indigent has now been returned to the individual counties, and there is no longer any uniform plan of supplying medical service for the indigent, and the greater part of such service is rendered without pay by physicians.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST; SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ALABAMA

Division Meeting at Wetumpka.—The Southeastern division of the Medical Association of the State of Alabama met at Wetumpka October 13 with the following speakers, among others: Drs. Jesse P. Chapman, Selma, "Evaluation of Diseases of the Colon"; Dan C. Donald, Birmingham, "Surgery of Undescended Testes with Special Reference to Torek's Operation"; Thomas M. Boulware, Birmingham, "Puerperal Sepsis"; Edgar F. Fincher and William A. Smith, Atlanta, "Diagnosis and Treatment of Brain Tumors"; David Henry Poer and Thomas S. Claiborne, Atlanta, thyroid diseases.

CALIFORNIA

Alumni Reunion.—The University of California Medical School will hold an alumni day November 18 with sessions at the San Francisco Hospital. Clinics will form a large part of the program, covering, among other subjects, pneumothorax, cerebral anoxemia, recent advances in treatment of acute coccid infections, dissecting aneurysm, use of iodine in toxic goiter and bronchiolitis in childhood.

Society News.—The program of the Los Angeles County Medical Association, November 3, was presented by the anesthesia section; the speakers were Drs. Douglas R. Drury and Arthur E. Guedel on "The Effect of Anesthetic Agents on the Liver" and "Postoperative Pulmonary Complications" respectively. At a meeting of the Military Surgeons of Southern California November 3 Drs. John R. Paxton and Ambrose S. Churchill, both of Olive View, spoke on "Surgery in Tuberculous Patients" and "Extrapleural Pneumothorax" respectively. The Alameda County Medical Association was addressed in Oakland October 17 by Drs. Charles H. DeVaul on "Glaucoma"; Daniel Crosby, "Medicine and Liberal Legislation"; Robert K. Cutter, Berkeley, "Use of Mixed Respiratory Vaccine," and Edith M. Meyers, Oakland, "Infection in the Newborn and Problems of Nursery Control." The Los Angeles Society of Neurology and Psychiatry was addressed October 19 by Drs. Clarence W. Olsen on "Constructive Apraxia"; Hans von Briesen, "Removal of Lipiodol After Myelography," and Johannes M. Nielsen, "Delayed Paralysis of Peripheral Nerves Due to Indirect Trauma." The Humboldt County Medical Society was addressed in Eureka October 6 by Drs. Perry A. Bonar, San Francisco, on urology, and Charles C. Falk Jr., Eureka, prostatic obstruction.

FLORIDA

Annual District Meeting.—The North Central Medical District Society held its second annual meeting in Gainesville October 27 at the Hotel Thomas. Dr. Thomas A. Snow, president of the Alachua County Medical Society, gave the address of welcome. In addition to officers of the state medical society, the following spoke:

Dr. Samuel C. Harvard, Brooksville, Cauterization of the Cervix.
Dr. Thomas H. Bates, Lake City, Intestinal Parasites Causing Surgical Conditions.
Dr. Walter J. Baker, Foley, Undulant Fever.
Dr. Edwin L. Scott, Ocala, Responsibility of the General Practitioner to the Crippled Children.

ILLINOIS

Death from Rabies.—According to the *Health Messenger*, a young woman in the village of Westville died September 17 from what the attending physician described as a typical attack of rabies. About four months previously the woman was scratched on the leg by a puppy that is believed to have been rabid at the time. Since the death of the woman, seven relatives who believed they had been exposed to rabies by the patient or the dog have taken the Pasteur treatment.

Chicago

Symposium on Air Conditioning.—A symposium on air conditioning for human occupancy will be presented in the auditorium of the Engineering Building, Chicago, 7:30 p. m. November 22 under the auspices of the Chicago chapter of the American Institute of Architects and some other organizations.

Society News.—Dr. Arnibald L. Hoyne will address the West Side Branch of the Chicago Medical Society November 17 on "Management of Scarlet Fever." The Chicago Medical Society was addressed November 2 by Drs. Max M. Peet, Ann Arbor, on "Surgical Treatment of High Blood Pressure," and Andrew C. Ivy, "Physiologic Aspects of the Surgery of High Blood Pressure." The Chicago Tuberculosis Society was addressed October 20 by Drs. Paul H. Holinger on "Bronchial Obstruction Produced by Cardiovascular Disease" and Willard Van Hazel, "Problems in Chest Surgery."

Discussion on Health of the Business Executive.—The department of industrial medicine of Northwestern University Medical School is sponsoring a dinner meeting at the Blackstone Hotel November 15, at which the theme of discussion will be "Health of the Business Executive—A Disturbing Industrial Problem." Dr. Robert M. Daley, medical director, Equitable Life Assurance Society, New York, and Dr. Edgar Van Nuys Allen, associate professor of medicine, Graduate School of Medicine, University of Minnesota, Rochester-Minneapolis, will be the speakers. Mr. O. E. Mount, chairman of the board of governors of the department of industrial medicine, will preside. Dr. Irving S. Cutter, dean of the medical school, will be the toastmaster.

KANSAS

Personal.—Dr. Walter P. Stoltenberg, Kinsley, has been appointed health officer of Kinsley County. Dr. Leonard S. Steadman, Junction City, has been appointed health officer of Geary County to succeed Dr. Robert J. Lanning, who recently resigned to enter private practice.

Society News.—Dr. James W. Shaw, Wichita, discussed "The Treatment of the Patient with Nervous Exhaustion" before the Sedgwick County Medical Society October 4; Dr. George F. Corrigan, Wichita, spoke October 18 on "Tophaceous and Pretophaceous Gout." Dr. William Walter Wasson, Denver, will discuss "The Anatomy, Physiology and Mechanics of the Chest as a Basis for the Study of Chest Diseases and Their Classification" before the Wyandotte County Medical Society November 15. The society was addressed November 1 by Drs. Harold V. Holter and Lewis G. Allen on "Cancer of the Fundus Uteri and Adnexa" and "Radiation Treatment of Inflammatory Diseases" respectively. Dr. James A. Fulton presented a "Statistical Report of 50,000 Anesthesias" at the meeting September 20, and Dr. Mervin J. Rumold discussed "Treatment of Appendiceal Peritonitis."

MARYLAND

Personal.—Dr. Leo V. Schneider, chief resident physician at the Tuberculosis Sanatorium, Glenn Dale, has been appointed associate clinical professor of medicine at Georgetown University School of Medicine, Washington, D. C.

Testimonial to Dr. Cullen.—Dr. Thomas S. Cullen, professor of gynecology, Johns Hopkins University School of Medicine, Baltimore, will be guest of honor at a dinner November 19 at the Southern Hotel commemorating his seventieth birthday. A native of Bridgewater, Ont., Dr. Cullen graduated from the University of Toronto Faculty of Medicine, Toronto, in 1890. He served as chairman of the Section on Obstetrics, Gynecology and Abdominal Surgery of the American Medical Association, 1914-1915, and has been a member of its Board of Trustees since 1929. He was president of the Southern Surgical and Gynecological Association in 1916. Dr. Cullen has contributed much to medical literature.

MASSACHUSETTS

Society News.—Dr. Abraham Myerson, Boston, addressed the Pentucket Association of Physicians October 13 on "Autonomic Pharmacology." Dr. Frederick W. O'Brien, Boston, addressed the society September 15 on "What X-Ray Therapy Can Be Expected to Accomplish." Dr. Philip E. C. Manson-Bahr, London, addressed the Harvard Medical Society, Boston, September 27 on "Diagnosis of Fevers in General Practice."

Medicolegal Conference.—About 100 persons registered for the first conference of the Massachusetts Medico-Legal Society at the Mallory Institute of Pathology, Boston City Hospital, Boston, October 4-5. Plans are now being considered to make the conference an annual event with a three or four day program instead of the two day program in this year's session. The society voted at this meeting to affiliate with the American Medico-Legal Association. Additional information may be obtained from Dr. William H. Watters, 270 Commonwealth Avenue, Boston.

MICHIGAN

Gifts to University.—Included among recent gifts to the University of Michigan, Ann Arbor, are the following: \$22,500 from the U. S. Public Health Service under the Social Security Act to be used for training public health personnel; \$8,000 from an anonymous donor for the study of infantile paralysis; \$2,000 from the National Foundation of Infantile Paralysis Research for Dr. Max Minor Peet to be used in prophylactic chemicals for combating epidemics; \$2,750 from the Du Pont Company, Wilmington, Del., for fellowships; \$1,000 from James G. Hayes, Pittsburgh, to be used by the regents at their discretion, and \$9,875 in assorted fellowships, scholarships and research grants from eleven different donors, newspapers reported.

Kellogg Foundation Increases Budget for Health.—The W. K. Kellogg Foundation, Battle Creek, will spend \$2,256,130 for health service and capital grants for new construction during the fiscal year 1938-1939, according to newspaper reports, almost doubling its allocation of \$1,130,902.75 for the year 1937-1938. The capital grants are divided into four classes, schools, hospitals, camps and youth buildings, and include the University of Michigan graduate dental schools and rural rehabilitation for 600 schools, it was stated. The foundation also sponsors health work in seven counties of the state, supplying the directors in charge of the health program. The counties are Calhoun, Allegan, Barry, Branch, Eaton, Hillsdale and Van Buren.

MINNESOTA

Public Health Dramatized at Annual Meeting.—The thirty-second annual session of the Minnesota Public Health Association will be held at the Nicollet Hotel, Minneapolis, November 18, with the Hennepin County Tuberculosis Association acting as host. At the annual Christmas Seal dinner Dr. William W. Bauer, Chicago, director of the Bureau of Health Education, American Medical Association, will be the guest speaker with Dr. Sidney A. Slater, Worthington, president of the public health association, as toastmaster. "Our Town Learns About Tuberculosis" is the title of a play to be presented with the following cast: Dr. Bauer, Miss Mable Johnson, R.N., and Miss Mary Lee, R.N. The skit illustrates how a school tuberculin testing program is sold to a community. Dr. Herman E. Hilleboe, St. Paul, director of the tuberculosis division, state board of health, will review the historical development of the fifteen public sanatoriums in Minnesota. Honor will be bestowed on the pioneer leaders in the establishment of the sanatoriums and life membership in the association will be conferred on them. Distinguished Service Christmas Seal Awards for 1937 will also be presented.

MISSOURI

Society News.—The St. Louis Medical Society was addressed October 4 by Drs. Anthony M. Tripodi on "Comparative Results of Partial Excision of the Pancreas with the Scalpel, Actual Cautery and Electrical High-Frequency Knife." A symposium on cannabis was presented by Charles Benjamin Holman, D.D.S., and Drs. John Auer and Lee D. Cady. Dr. Virgil Holland Moon, Philadelphia, addressed the Kansas City Academy of Medicine October 14 on "Shock: Its Mechanism—Pathology and Early Diagnosis." The academy was to be addressed November 11 by Dr. Shields Warren, Boston, on "Pathology of Diabetes Mellitus."—At a special joint meeting of the medical societies of Jefferson, Franklin and St. Louis counties in St. Louis October 21 Drs. Oscar F. Bradford, Columbia, and Paul R. Fletcher discussed "Various Phases of Preventive Obstetrics and Pediatrics."—The St. Louis County Medical Society was addressed September 28 by Dr. John D. Hayward on "Presacral Sympathectomy for Dysmenorrhea."

NEW JERSEY

Personal.—Dr. Harry B. van Dyke, head of the division of pharmacology at the Squibb Institute for Medical Research, New Brunswick, has been appointed honorary professor of physiology at Rutgers University. He will also serve as research consultant in the bureau of biological research and will be a member of the graduate faculty.—Dr. Hymen I. Goldstein, Camden, has been elected a corresponding member of the Royal Italian Society of Gastro-Enterology of Rome.

District Meeting in Bridgeton.—The Fifth Councilor District of the Medical Society of New Jersey will hold a meeting in Bridgeton November 15 with the following speakers: Dr. Hilton S. Read, Atlantic City, "Evolution, Not Revolution, in Organized Medicine"; Dr. William J. Carrington, Atlantic City, "What Changes Will There Be in the

Practice of Medicine in 1939?" and Allen A. Stockdale, D.D., New York, "Foundations of American Life." Legislators of the five counties in the district have been invited as guests.

Prosecutions by State Board.—The New Jersey board of medical examiners recently reported the following prosecutions during the past few months:

Harry A. Kaplan, Camden, naturopath, paid the penalty for practicing without a license.

Joseph West, Camden, who called himself a "doctor of spinal therapeutics," paid the penalty for a second violation of the medical practice act.

George Lezenby Sr., Camden, an "electrotherapist," paid the penalty for a third violation of the medical practice act.

T. Roberts Hill, Camden, who held himself out as a "foot correctionist," Morris Krichman, a pharmacist of Maple Shade, and Philip Mitter, Newark, a naturopath, were found guilty of practicing medicine without a license.

Samuel Talpins, David Samuels and Jacob J. Kohn, Newark pharmacists, George Maza, Newark chiropractor, Abraham Shavelson, East Orange pharmacist, Mary Bennett, Newark, who was prescribing "Liquid Life," and Joseph R. Messina, Newark, who held himself out as a scalp specialist, paid penalties for practicing medicine without licenses.

John Grassi, West New York pharmacist, was found guilty of practicing medicine without a license.

Alfred W. Reid, Collingswood, unlicensed chiropractor, found guilty of a second violation of the medical practice act.

NEW YORK

Society News.—At the annual meeting and dinner of the Madison County Medical Society, Oneida, October 13, the speakers were the following Syracuse physicians: Drs. Carlton C. Curtiss, "The Practitioner Looks at State Medicine"; Earle E. J. Mack, "Acute Infectious Mononucleosis"; Gordon D. Hoople, "Diagnostic Use of the Bronchoscope and Esophagoscope," and Tracy L. Bryant, "Gas Bacillus Infection."—Dr. Frank H. Lahey, Boston, addressed the Medical Society of Westchester County, October 18, on "The Newer Developments in Thyroid States."—Dr. Francis M. Rackemann, Boston, addressed the Medical Society of the County of Nassau, Mineola, October 25, on "Allergy in General Practice."—Dr. Irving J. Walker, Boston, addressed the Warren County Medical Society, Glens Falls, October 12, on appendicitis.—Dr. Leon Unger, Chicago, addressed the Medical Society of Jamestown October 27 on "Allergy in General Practice."

Court Forbids State Board to Examine Foreign Physicians.—The State Board of Regents has been ordered to endorse the licenses of foreign physicians wishing to practice in New York if the physicians submit satisfactory proof of their qualifications. The order was contained in a decision by Supreme Court Justice Sydney Foster in a test case involving Drs. Julius Levi, Paul Erlanger and Maximilian Lewitter, brought by Irving Mariasch of the American Citizenship Committee of the New York County Lawyers Association after the board had refused to endorse the licenses of these physicians. About 100 physicians are affected by the order. In his decision Justice Foster said: "The statute does not require any examination. The regents' rule contravenes the statute and fixes a standard beyond that contemplated by the legislature. Under this principle it became the duty of the board to endorse petitioner's license if he submitted satisfactory proof that the same was issued on requirements substantially equivalent to those in force in this state at the time and also that he had practiced lawfully and reputably for the prescribed period."

New York City

Second Harvey Lecture.—Dr. Alexander Ashley Weech, associate professor of diseases of children, Columbia University College of Physicians and Surgeons, will deliver the second Harvey Lecture of the current series at the New York Academy of Medicine November 17. His subject will be "Significance of the Albumin Fraction of Serum."

Symposium on Diseases of the Skin.—Lectures on diseases of the skin will be presented by the Medical Society of the County of Queens November 14-17 at the society's building. Lecturers in the symposium will be Drs. Ida J. Mintzer, "Common Skin Conditions"; Charles S. Miller, "New Growths of the Skin"; Joel Schweig, "Parasitic Diseases," and Rudolph Boenke, "Therapeutics of Common Skin Diseases."

Personal.—Dr. John H. R. Barry, for thirty years assistant sanitary superintendent for the borough of Queens, has retired from the city service, having reached the age limit.—Dr. Francis Peyton Rous of the Rockefeller Institute for Medical Research received the honorary degree of doctor of science at the opening of the University of Michigan Medical School, Ann Arbor, October 1, when he delivered the convocation address.

Fraternity Sponsors Lectures.—The Tau (Cornell) chapter of the Nu Sigma Nu Medical Fraternity is inaugurating a series of annual lectures on subjects of general interest to

the medical profession. Dr. Louis V. Hamman, associate professor of medicine, Johns Hopkins University School of Medicine, Baltimore, delivered the first lecture of the series November 10 in the auditorium of the Cornell University Medical College, 1300 York Avenue, on "Spontaneous Interstitial Emphysema of the Lung."

Cornerstone Laid for Health Center.—Mayor La Guardia, Nicholas Murray Butler, Ph.D., president of Columbia University, Dr. John L. Rice, health commissioner, and Dean Sage, president of the board of managers of Presbyterian Hospital, were the speakers at a ceremony for laying the cornerstone of the Washington Heights Health and Teaching Center October 17. The new center is one of five to be affiliated with the city's five medical schools for teaching public health. It will be operated in conjunction with the College of Physicians and Surgeons of Columbia University.

Another Doctors' Orchestra Organized.—About fifty physicians and dentists under the chairmanship of Dr. Israel Leopold Glushak have organized the Doctors' Orchestral Society with Ignatz Waghalter, formerly music director of the Berlin Charlottenburg Opera House, as conductor. Rehearsals are under way. The Wurlitzer Music Company, 120 West Forty-Second Street, has extended to the society the privilege of using its auditorium for rehearsals once a week. Membership is still open for enrolment; physicians and dentists interested in joining the orchestra may communicate with Dr. Glushak, 1 West Eighty-Fifth Street, New York.

NORTH CAROLINA

District Meetings.—The Seventh District Medical Society held a meeting in Charlotte October 18 with Dr. Edgar G. Ballenger, Atlanta, as the guest speaker on "Resistant Urinary Infections." Other speakers were Drs. Jackson T. Ramsaur, Cherryville, on "Female Sex Hormone"; James Lee Robinson Jr., Gastonia, "Acute Mesenteric Lymphadenitis," and Lester A. Crowell Jr., Lincolnton, "Practical Handling of Adult Uncomplicated Diabetes Mellitus." Dr. James Buren Sidbury, Wilmington, president of the Medical Society of North Carolina, spoke on the work of the state society.—Dr. David T. Smith, Durham, was the guest speaker at a meeting of the Ninth District Medical Society in Thomasville, September 29, on "Treatment of Local and Generalized Staphylococcus Infections with Staphylococcus Toxoid and Staphylococcus Antitoxin." Others on the program included Drs. Edward D. Andrews and George F. Busby, Salisbury, on "Thrombocytopenia in Infancy"; Edwin J. Cathell, Lexington, "Review of Recent Literature on Sulfanilamide, with a Case Report on Its Use in Peritonitis," and Reno K. Farrington, Thomasville, "Chronic Fibrous Incapsulated Peritonitis (Agglutinative Peritonitis)." Dr. James Buren Sidbury, Wilmington, president of the state medical society, also addressed the meeting.

OHIO

Society News.—Dr. Elmer L. Sevringhaus, Madison, Wis., addressed the Academy of Medicine of Cincinnati October 18 on "Pituitary Therapy in General Practice." Dr. Roy Glenwood Spurling, Louisville, Ky., addressed the academy October 4 on "Low Intraspinal Lesions as a Cause of Low Back and Sciatic Pain."—Dr. Roscoe G. Leland, director, Bureau of Medical Economics, American Medical Association, Chicago, addressed the Summit County Medical Society, Akron, October 4, on "The Trend Toward the Socialization of Professions."—Dr. John A. Toomey, Cleveland, addressed the Stark County Medical Society, Canton, November 10, on "Specific Prevention and Treatment of the Acute Exanthems."—A symposium on medical economics was presented before the Academy of Medicine of Toledo and Lucas County October 7 by Drs. Barney J. Hein, Frederick M. Douglass and William A. Neill.

PENNSYLVANIA

"Medicine Man" Convicted.—A concessionaire at the Lehigh fair selling a "medicine" was arrested, tried and convicted within three days in a drive of state authorities against fraudulent medicines, the state board of pharmacy reports. The man is said to have claimed that the medicine was a cure for rheumatism, sciatica, stomach ailments, nervousness and other diseases. The sample was taken to the laboratory of the state board of pharmacy at Harrisburg and found to be psyllium. Sentence was suspended on payment of the costs, about \$19, and the concessionaire was warned to stop selling fake medicines in Pennsylvania.

Philadelphia

First de Schweinitz Lecture.—Dr. Edward Jackson, Denver, will deliver the first de Schweinitz lecture of the section on ophthalmology of the College of Physicians of Philadelphia November 17 on "The Development of Ophthalmology in One Lifetime." The lecture was established in honor of Dr. George E. de Schweinitz, who died August 22.

Emergencies and the Profession.—The meeting of the Philadelphia County Medical Society November 9 was devoted to discussion of "National and Local Emergencies and the Medical Profession." The speakers were Col. Charles P. Stahl, Lancaster, Pennsylvania National Guard, on "The Medical Profession and the National Guard"; Brig. Gen. Wallace DeWitt, commandant, Army Medical Center, Washington, D. C., "The Doctor and the Army"; Comdr. William J. C. Agnew, San Diego, Officer in Charge of Reserve Affairs, Bureau of Medicine and Surgery, U. S. Navy, Washington, "The Doctor and the Navy," and Dr. Hubley R. Owen, chief surgeon, Philadelphia bureau of fire and police, "The Doctor and Local Catastrophic Emergencies."

Pittsburgh

Lectures on Diabetes.—Two lectures a year on diabetes are to be given in Pittsburgh under the terms of a gift by Miss Emilie Renziehausen in memory of her brothers. In 1937 Miss Renziehausen gave a fund of a million dollars to the Children's Hospital for research on diabetes. Dr. Charles H. Best, professor of physiology at the University of Toronto, will deliver the first lecture December 5 at the Mellon Institute on "Historical and Recent Development of the Insulin Situation."

SOUTH CAROLINA

Founder's Day at South Carolina.—The Medical College of the State of South Carolina, Charleston, observed Founder's Day, November 3. The speakers were:

Dr. Hugh P. Smith, Greenville, Sprue.
Dr. Daniel L. Smith, Spartanburg, Allergy in Children.
Dr. Douglas Jennings, Bennettsville, Extra-Uterine Pregnancy.
Dr. James J. Ravenel, Charleston, Renal Calculi.
Dr. Olin B. Chamberlain, Charleston, subject not announced.

Dr. Frederic M. Hanes, professor of medicine, Duke University School of Medicine, Durham, N. C., delivered the Founder's Day address at an evening banquet on "The Position of the Medical School in the Newer Concepts of Medical Practice."

District Meetings.—The annual meeting of the Seventh District Medical Association was held at Manning September 15 with the following speakers, among others: Drs. William H. Kelley, Charleston, "Nicotinic Acid in Treatment of Pellagra"; Virgil P. W. Sydenstricker, Augusta, Ga., "Pellagra," and James Heyward Gibbs, Columbia, "The Menace of Tick-Borne Diseases in South Carolina."—The Fifth District Medical Society met in Winnsboro October 26 with the following speakers, among others: Drs. George H. Bunch, Columbia, on "Acute Appendicitis"; Lucius Emmett Madden, Columbia, "Coronary Thrombosis," and James C. McLeod, Florence, "Head Injuries." Dr. James R. DesPortes, Fort Mill, president of the South Carolina Medical Association, also made an address.

TEXAS

Changes in Health Officers.—Dr. Durwood L. Dodd has been appointed health officer of Austin, succeeding Dr. Francis Banner Gregg.—Dr. Lyman T. Cox, El Paso, has been appointed health officer of the city and county of El Paso, succeeding Dr. John W. Tappan, it is reported.—Dr. Arthur Gleckler, Sherman, recently succeeded Dr. Buford A. Russell as health officer of Grayson County.

Society News.—Drs. Maurice P. S. Spearman and Willis W. Waite, El Paso, addressed the El Paso County Medical Society September 12 on "Bronchoscopy as an Aid in General Diagnosis" and "Syphilitic Endocarditis of the Mitral Valve" respectively.—At a meeting of the Dallas County Medical Society October 27 the speakers were Drs. Casey E. Patterson, on "Treatment of Asthma"; Thomas E. Smith, "Hypertrophic Anal Papillae," and James T. Mills, "Surgical Treatment of X-Ray Burns and Nevi."

VIRGINIA

Society News.—Dr. Samuel A. Cosgrove, Jersey City, N. J., addressed the Virginia Peninsula Academy of Medicine, Newport News, September 19, on "Toxemias of Late Pregnancy." Dr. Louis H. Douglass, Baltimore, was the guest speaker at the annual meeting of the Virginia Obstetrical and Gynecological Society October 5 in conjunction with the annual

meeting of the Medical Society of Virginia in Danville, on "The Problem of the Posterior Occiput."—The Rockbridge County Medical Society was reorganized September 13 with Drs. Francis L. Thurman, Buena Vista, as president; Jesse Hugh Bailey, Brownsburg, vice president, and Edmund P. Tompkins, Lexington, secretary.

WASHINGTON

Personal.—Dr. Harmon T. Rhoads Sr., Everett, has been appointed surgeon to the Wilkins-Lincoln Ellsworth expedition to the South Pole.—Dr. Ralph Gregg of the U. S. Public Health Service, recently stationed in Tacoma, has been assigned to be health officer of Tacoma, succeeding the late Dr. Samuel M. Creswell.

Hospital News.—Dr. Simeon T. Cantril, Chicago, has been appointed to direct the cancer institute of Swedish Hospital, Seattle, with Mr. Herbert N. Parker, formerly of Manchester, England, as physicist. Dr. Cantril succeeds Dr. John E. Wirth, who will join the staff of the U. S. Public Health Service to conduct research under the cancer program authorized by the National Cancer Institute Act of 1937. John E. Rose, physicist since 1934, will also go to the public health service.

Society News.—Dr. Robert L. King, Seattle, addressed the Pierce County Medical Society, Tacoma, September 13, on "Symptoms and Signs of Rheumatic Fever."—Dr. Robert W. Langley, Los Angeles, showed a color film entitled "Heart Sounds, a Clinical Experiment in Sound Photography" at a meeting of the King County Medical Society, Seattle, October 3. Drs. Darrell G. Leavitt and Nathan K. Rickles addressed the society October 17 on "Surgical Treatment of Tuberculous Joint" and "Metrazol Therapy" respectively.—Drs. George H. Anderson, Spokane, and Edgar Murray Burns, Portland, addressed the first fall meeting of the Walla Walla Valley Medical Society, Walla Walla, October 13, on "Osteoarthritis of the Spine Causing Symptoms of Visceral Disease" and "Psychotherapeutic Ideas Applicable to General Medicine" respectively. Drs. Herbert F. Traut, New York, and George W. Pierce, San Francisco, will address the society November 14 on "Recent Advancements of Endocrinology" and "Repair of Nerves and Tendons from Traumatic Injuries" respectively.—Dr. Wallace E. Herrell, Rochester, Minn., addressed the Spokane County Medical Society, Spokane, October 13, on "Management of Ovarian Dysfunction with Reference to Diagnostic Aids."

WISCONSIN

Marquette Requires County Society Membership.—Members of the faculty of Marquette University School of Medicine, Milwaukee, will henceforth be required to hold membership in the Medical Society of Milwaukee County and the State Medical Society of Wisconsin. A motion to this effect was adopted by the executive faculty October 12 and approved by the president of the university. Every member of the faculty who is qualified to join the medical society must do so to retain his position. In addition, every person proposed for appointment who is qualified to belong to the society must present evidence of membership as a qualification for appointment to the medical school.

Society News.—Dr. M. Herbert Barker, Chicago, addressed the Rock County Medical Society, Janesville, September 27, on "Types of Hypertension and Their Treatment."—Drs. Wallace H. Steffensen, Grand Rapids, Mich., and Joseph L. Ransohoff, Cincinnati, addressed the Milwaukee Society of Clinical Surgery October 25 on "Management of Free Skin Grafts" and "Surgical Relief of Pain in Angina Pectoris" respectively.—Dr. William A. O'Brien, Minneapolis, and Mr. James H. Baker, executive secretary of the Hennepin County Medical Society, Minneapolis, addressed the Polk County Medical Society September 22 on "Medical News from the Standpoint of Physicians and Newspapermen."

HAWAII

Society News.—Dr. Walter C. Alvarez, Rochester, Minn., presented a series of lectures on gastro-enterology before the Honolulu County Medical Society recently.

New Mental Clinic.—A clinic for mental hygiene was recently established in Honolulu to serve the territory of Hawaii. Dr. Franklin G. Ebaugh, Denver, supervised the organization. A unit at Queen's Hospital has been given over to the clinic to provide hospitalization and treatment facilities. Dr. Edwin E. McNiel, New York, was to take charge of the clinic October 18. Steps were recently taken to initiate mobile mental health clinics to serve these islands.

GENERAL

Child Study Association Fifty Years Old.—The Child Study Association of America will observe its fiftieth anniversary November 14-15 with a conference at the Hotel Roosevelt, New York, followed by a three day institute. The conference theme will be "What do we know today about better methods of rearing children and developing better family life that we did not know a half century ago?" Headquarters of the association are at 221 West Fifty-Seventh Street, New York.

Examinations in Obstetrics and Gynecology.—The next written examination and review of case histories for group B candidates will be held in various cities of the United States and Canada February 4. Applications for this examination of the American Board of Obstetrics and Gynecology must be filed on an official application form in the office of the secretary at least sixty days prior to this date (or before December 4). The general oral, clinical and pathologic examinations for all candidates (groups A and B) will be conducted by the entire board, meeting in St. Louis May 15-16, 1939, immediately prior to the annual session of the American Medical Association. Applications for admission to group A examinations must be on file in the secretary's office by March 15, 1939. For further information address Dr. Paul Titus, Secretary, 1015 Highland Building, Pittsburgh.

Meeting on Obstetrics and Gynecology.—The seventh annual meeting of the Pacific Coast Society of Obstetrics and Gynecology will be held at the Ambassador Hotel November 30-December 3 under the presidency of Dr. Raymond E. Watkins, Portland, Ore. The speakers will include:

Dr. Virgil E. Dudman, Portland, Arrhenoblastoma and Digerminoma.
Dr. Margaret Schulze, San Francisco, Granulosa Cell Tumors and Brenner Tumors.
Drs. Albert Mathieu and Albert W. Holman, Portland, Induction of Labor in Toxemia of Pregnancy.
Dr. Bernard J. Hanley, Los Angeles, Sulfanilamide in Obstetric Infections.
Dr. Ludwig A. Emge, San Francisco, Relation of Hormones to Carcinogenesis.

The program will also include a symposium on hemorrhage in pregnancy.

American Society of Tropical Medicine.—The thirty-fourth annual meeting of the American Society of Tropical Medicine will be held November 15-18 in Oklahoma City in conjunction with the meeting of the Southern Medical Association. Dr. Richard P. Strong, Boston, will deliver the third Charles Franklin Craig Lecture Tuesday afternoon, November 15, on "Progress in the Study of Infections Due to Bartonella and Rickettsia." Dr. Mark F. Boyd, Tallahassee, Fla., will deliver his presidential address at a luncheon Thursday November 17, on "A Résumé of Studies on the Relation of the Malaria Parasites to Their Hosts." Another feature will be a symposium on "Newer Clinical Aspects of Deficiency Diseases," presented by Drs. John B. Youmans, Nashville, Tenn.; George C. Shattuck, Boston; Tom D. Spies and William B. Bean, Cincinnati, and Alfred C. Reed, Leonid S. Cherney, Charles M. Wheeler, Ph.D., San Francisco, and William J. Dann, Ph.D., Durham N. C.

Society News.—Dr. Edward L. Jenkinson, Chicago, was chosen president-elect of the American Roentgen Ray Society at its recent annual meeting in Atlantic City, N. J., and Dr. John W. Pierson, Baltimore, was inducted into the presidency. Other officers include Drs. Cornelius G. Dyck, New York, vice president; James B. Edwards, Leonia, N. J., treasurer, and Carleton B. Peirce, Montreal, secretary. The next meeting of the society will be in Chicago September 19-22.—Dr. John C. Dessloch, Rochester, N. Y., was chosen president-elect of the Associated Anesthetists of the United States and Canada at the annual meeting in New York in October. Dr. F. Hoeffer McMechan, Rocky River, Ohio, was reelected secretary. The next meeting will be held in St. Louis, May 15-21, 1939.—Dr. Henry W. Cook, Minneapolis, medical director of the Northwestern National Life Insurance Company, was elected president of the Association of Life Insurance Medical Directors at the annual meeting in New York October 20. Drs. Harold M. Frost, Boston, and Donald B. Cragin, Hartford, Conn., were elected vice presidents, and Dr. Edwin G. Dewis, Interlaken, N. J., secretary.—Dr. Charles D. Mitchell, Whitefield, Miss., was named president-elect of the Southern Psychiatric Association at its annual meeting in Atlanta October 11. Dr. Charles S. Holbrook, New Orleans, was installed as president, Dr. Whitman C. McConnell, St. Petersburg, Fla., was elected vice president and Dr. Newdigate M. Owenby, Atlanta, reelected secretary.

Foreign Letters

LONDON

(From Our Regular Correspondent)

Oct. 22, 1938.

The State and Medical Research

Sir Edward Mellanby, secretary of the Medical Research Council, delivered the Harveian oration at the Royal College of Physicians on "The State and Medical Research." He said that private endowment of research had no proud history in this country, although there had been fine exceptions in the case of medicine. As to government support, it took a great war to make the government set up the Department of Scientific and Industrial Research in 1915. The Medical Research Committee was originated in 1913 in connection with the national health insurance act. This arrangement was terminated in 1919, and the Medical Research Council received its present title and constitution in 1920. It is financed with money provided by the government. During the present century there have been two rapid increases in medical research activity, running side by side: the one in this country, organized and to a large extent financed by the state, the other in the United States, richly endowed and controlled by private interests. Each had already produced a good harvest. The recent Nuffield scheme, started at Oxford, was possibly an indication that private persons would in the future regard the endowment of research here as more worthy of their support. The most limiting factor in all research activity, but especially in medical research, was personnel. The number of people who were trained for and capable of doing work of this type was not large. By various means the council was trying to increase their number.

Speaking of the work of the National Institute for Medical Research, Mellanby said that it had always reached the highest standard. One aspect of it of particular interest to the physician was the biologic standardization of drugs. In this the institute led the world and had rendered a great service to mankind. Another line of policy was the placing of units of research in different institutions, and this had shown great developments in recent years. Short of a catastrophic change, which might upset or even destroy national life, the future was bright. There was no doubt that more and more knowledge, giving control, both preventive and curative, of disease would be obtained. The difficulty he foresaw was not that of obtaining knowledge but of its application to human needs. This would depend on the education and wisdom of individuals. Without an enlightened public opinion the average person would do nothing to save himself, and the state would do less. There was a shocking neglect in this country of using the available knowledge for the prevention of diphtheria.

The Importance of Bacteremia

In an address to the Nottingham Medico-Chirurgical Society, Prof. J. A. Ryle pointed out that bacteria enter the circulation more readily and more often than is supposed and that this fact is important in recognizing and understanding many diseases. Blood infection may be innocent or may be serious. Ryle distinguishes bacteremia from septicemia. Bacteremia implies nothing more than the presence of organisms in the blood and is a pathologic observation rather than a clinical state. But septicemia is characterized by fever, rigors and a tendency to metastatic lesions and it carries a grave prognosis. It is due to, but is not synonymous with, bacteremia, which can occur in the absence of septicemic symptoms. Although meningococci and pneumococci bacteremia may be complicated by rigors and metastatic infection, the term septicemia should be reserved for streptococci and staphylococci infections.

Osteomyelitis, perinephric abscess and some other staphylococci lesions were long considered local diseases, with no

reference to the primary focus or the pathways of infection or the possibility of other foci. But in fatal staphylococci septicemia the necropsies showed that the bones, the kidney, the lungs and the heart were among the selected sites for metastatic infection. Clinical study reveals a primary focus in the shape of a boil, carbuncle or infected abrasion in more than three fourths of cases of remote and deeply seated staphylococci infections. Perinephritis has been shown to represent a spread of infection from a metastatic cortical abscess which has perforated the renal capsule. Osteomyelitis and renal and prostatic abscesses may develop without any intervening septicemic illness. As these tissues can be reached only through the blood stream, a relatively benign bacteremia must have occurred, although it is usually too late to obtain a blood culture. Staphylococci bacteremia is more common than is supposed. Many patients with recurring furunculosis must pass through unrecognized phases of transient hemic infection, and obscure fevers can sometimes be shown to be due to this cause.

In a considerable proportion of cases of pneumonia, pneumococci may be grown from the blood during the early stages and in a smaller proportion throughout, without carrying a bad prognosis. A hemic infection can be inferred in the cases complicated by meningitis, peritonitis or arthritis. In meningitis the meningococcus has been grown from the blood. The suddenness of the disease in many cases, the petechial rash and the occasional arthritis and pericarditis all indicate blood infection. *Streptococcus viridans* has its abode in the mouth and particularly in tooth sockets. It is the commonest organism found in the blood in subacute endocarditis. The accident of a bacteremia in a subject with damaged or anatomically abnormal valves determines the disease. Okell and Elliott have shown how slight trauma may drive organisms from the dental sockets into the blood stream. Within a few minutes after the extraction of teeth from a septic mouth a transient streptococci bacteremia was found in 75 per cent of the cases. Even with no obvious disease of the gums, a transient bacteremia followed in 34 per cent. Of 110 patients with septic mouths 10.9 per cent were found to have a streptococci bacteremia irrespective of operative intervention.

Thus a bacteremia from trivial causes or accompanying a serious local infection is more common than is generally supposed. Ryle recommends that a blood culture should be performed in every case of typhoid or of streptococci or staphylococci septicemia, whenever bacterial endocarditis is possible, in any case presenting rigors, and in any sustained or intermittent fever for which no adequate local or nonbacterial cause can be discovered. Its repetition with colony counts may give useful information with regard to the progress of the disease and assist in the study of the effects of chemotherapeutic agents.

Polycyclic Hydrocarbons Which Produce Cancer

At the recent meeting of the British Association, Prof. J. W. Cook, F.R.S., pointed out that a considerable group of polycyclic hydrocarbons were known to be carcinogenic. They differed widely in the rapidity with which they produced tumors. In animals cancer of the skin, liver, uterus, prostate, stomach and brain could be so produced. The manner in which these carcinogenic agents transformed normal into malignant cells was unknown, but some of the factors of molecular structure that were associated with carcinogenic activity could be stated. Thus the meso positions (9 and 10) of the benzantracene molecule were favorable for carcinogenic activity, and the 9:10-dimethyl compound with a methyl group in each of these meso positions, recently synthesized by Bachmann at the University of Michigan and tested at the Royal Cancer Hospital, had proved to be the most potent cancer-producing compound yet produced. In mice it gave rise to cancers of the skin, which first appeared as multiple warts within thirty-five days. Excepting the compound 5:9:10-trimethyl-1:2-benzanthracene, no other sub-

stance produced cancer in less than double this time. The compounds coming next in carcinogenic power were methylchloranthrene and benzpyrene, for which the latent periods were seventy-five and 100 days respectively. Methylchloranthrene could be prepared in the laboratory by comparatively simple reactions from cholesterol and bile acids. It was conceivable that similar transformations could occur in the body, but evidence of this was lacking.

PARIS

(From Our Regular Correspondent)

Oct. 15, 1938.

Surgical Treatment of Tumors of the Lung

The subject of the third symposium at the recent meeting of the International Surgical Society was the surgical treatment of pulmonary cysts and tumors. The first paper was by Dr. Costantini of Algiers, who said that the two great dangers in pulmonary surgery were pneumothorax and collapse of the lung. The latter, as the result of vagosympathetic reflexes, may be followed by fatal disturbance of the cardiac innervation. Of less importance but not to be overlooked are two other factors, elasticity of the lungs and the condition of the mediastinum, i. e. whether it is mobile or rigid. As a rule, a pneumothorax is well tolerated by younger persons, complications being most often observed after the age of 50, also in patients who present the cardiac effects of a chronic infection or of a cancerous cachexia. Chilling of the lung also plays an important part in the production of shock and should be guarded against by giving large quantities of dextrose solutions at 40 C. (104 F.) by the drop method before operation and the use, during the operation, of large, hot gauze packs and sponges. The combined use of the intratracheal method of anesthesia and of nitrous oxide is the best way to prevent pulmonary collapse. These should be supplemented by giving both atropine and ephedrine. Costantini believed that excessive bronchial secretion during the operation could be best combated by placing the patient in a moderate Trendelenburg position. Ligation of the large bronchi and of the pulmonary artery is generally well tolerated but reflex cessation of cardiac action may occur during ligation of the artery. Bronchial fistulas usually heal spontaneously. A preoperative pneumothorax is an efficacious method to prevent a pulmonary collapse. After a few months the opposite lung will completely compensate the effects of a pneumectomy. He warmly recommended exploratory thoracotomy for diagnostic purposes.

The second paper on cysts and tumors of the lung was read by Dr. José Arce of Buenos Aires. With the exception of cases of echinococci cysts of the lung, which should be operated on in one stage, it is preferable to establish pleuropulmonary adhesions before operating on patients with pulmonary suppuration. After three ribs have been resected, a gauze pack is firmly inserted in such cases as a preliminary step. The speaker warmly endorsed the recommendation of Dr. Costantini as to the value of preoperative pneumothorax in the prevention of pulmonary collapse. Preference was given to local, regional or spinal anesthesia but it is impossible to avoid the use of general anesthesia in very difficult cases and also when positive pressure was used. Malignant tumors of the lung are more frequently encountered than those of the benign type. Dr. Arce prefers a three step operation and, during the final stage, complete removal of the lung. Of twenty-seven cases of cancer only twelve were considered to justify a radical procedure. Three lobectomies and nine pneumectomies were done, with eleven deaths.

The third paper was by Dr. Forni of Venice, who stated that an operative indication existed in only about 10 per cent of the cases of cancer of the lung. After a critical analysis of all reported cases, his conclusions were that a complete one step

pneumectomy through an anterior incision is the operation of choice in tumors of the larger bronchi and that a lobectomy preceded by pneumothorax and phrenicectomy should be done for circumscribed tumors in the smaller bronchi. Of thirty-three pneumectomies (thirty in one step and three in two steps) ten are cured. In only three of these ten cases has a year elapsed since the operation. Three patients show signs of recurrence and twenty died following the operation. Of sixty-two lobectomies, thirty-eight of which were one step operations, there are sixteen cures, thirteen operative deaths and eleven fatal recurrences. In the other twenty-four lobectomies, in which a two or three step procedure was employed, there were nine cures, ten operative deaths and five recurrences.

Dr. Baggio of Pisa, in the fourth paper, stated that he preferred a two step operation in echinococci cysts of the lung and the use of a short drainage tube for a very short time after operation in order to avoid cutaneous fistulas of long duration.

The discussion on the present status of pulmonary surgery was opened by Mr. Tudor Edwards of London, who limited operative intervention to cancer of the bronchi. In 60 per cent of his cases the search for cancer cells, according to the Dudgeon technic, had been positive. He warmly recommended the use of preoperative pneumothorax, because a large exposure is needed in order to establish pleural adhesions and carry out an extensive pneumectomy as close as possible to the bifurcation of the trachea with separate ligation of the bronchial vessels. The percentage of cures is still very small. Of 172 persons with cancer of the bronchi seen over a period of thirty months, twenty-eight were subjected to an exploratory operation; only thirteen have survived a pneumectomy but six have lived more than six months.

Dr. Stuart W. Harrington reported the results of 121 operations for intrathoracic tumors at the Mayo Clinic. There were nineteen cysts of the lung or anterior mediastinum, of which thirteen were of the teratoid type. It was possible to remove the cyst completely in sixteen cases and to do a pneumectomy in two cases. In one, a malignant condition, the entire tumor could not be removed. In seventeen of the eighteen cases in which complete removal was possible cure apparently resulted, the interval since the operation not being stated. The remaining patient showed signs of recurrence six months after operation.

Dr. James M. Mason of Birmingham, Ala., reported a case of bronchiogenic cancer of the lower lobe of the right lung in which lobectomy had been done with apparent cure in spite of a postoperative pyopneumothorax.

Drs. Dargent and Bérard of Lyons called attention to the difficulties encountered in the early diagnosis of a primary cancer of the lung. An anteroposterior and a lateral bronchogram, as well as the more recent roentgenographic method of diagnosis in sections or tomography have been of great aid. An exploratory operation should not be postponed until pleural adhesions, which are usually of malignant character, have formed. Irradiation with radium is preferable to an incomplete operation, when pleural adhesions exist. Some types of tumors of the lung are very radiosensitive and even in the radioresistant forms irradiation relieves both the pain and the dyspnea.

Dr. Chiarolanza of Naples stated that the mortality following operations for tumors of the lung is still very high. Twenty fatalities occurred in thirty-three pneumectomies, twenty-three fatalities in sixty-three complete lobectomies and twenty-four fatalities in seventy-three atypical operations. The recurrence statistics are equally unfavorable.

THE NEXT INTERNATIONAL SURGICAL CONGRESS

The next meeting of the International Surgical Society will take place at Stockholm during the summer of 1941. At the recent meeting in Brussels Leopold Mayer of Belgium was elected president, and Alessandri of Italy, Arce of Argentina,

Lenormand of France and G. Grey-Turner of England vice presidents. Sir John d'Arcy Power of London was elected honorary president and Prof. Verhoogen of Brussels chairman of the permanent committee. The subjects to be discussed at the 1941 congress include (1) postoperative complications, (2) surgical treatment of pulmonary tuberculosis and (3) sequelae and complications of operations on the biliary tract.

Physical Examination of First Year Students

The dean of the Faculté de médecine, Professor Tiffenau, has just sent a notice to every student who has been matriculated for the present school year to go to the Léon Bourgeois dispensary for a complete examination. Although the latter is not obligatory, every student is urged to have at least a radioscopic examination of the chest and tuberculin tests made, because it has been found that a number of students and pupil nurses show evidences of incipient tuberculosis soon after being exposed to infection while working in wards to which patients with some form of the disease are admitted.

International Union Against Cancer

The International Union Against Cancer, which aims to coordinate the work of all organizations engaged in the study of cancer and the means to combat it, has arranged an international cancer week from the 23d to the 30th of November in fifty countries. During this cancer week the first meeting in Paris will be held at the Sorbonne, November 23. At the international cancer reunions in Paris a number of papers will be read to commemorate the discovery of radium, electrons, x-rays and hertzian waves.

BERLIN

(From Our Regular Correspondent)

Oct. 3, 1938.

Malignant Anemia

Sternal puncture has proved its worth as an important method of examination in the differential diagnosis of diseases of the blood. The procedure is valuable for determination of granulocytopenia, purpura haemorrhagica and similar pathologic conditions in which the formation of a particular type of bone marrow cells is disturbed. It is equally valuable in various forms of anemia characterized by damage to granulocytes and megakaryocytes. In a condition observed of late with relative frequency, panmyelophthisis, all three types of marrow cells are involved. Another distinct entity observed more frequently in recent years than before is characterized by hyperchromic anemia and thrombopenia and by proliferation of the myeloblasts of the bone marrow. Analogous results in the sternal puncture (material isolated nucleated erythrocytes, absence of megakaryocytes, abundance of myeloblasts, isolated myelocytes and extremely few neutrophils) may be observed in no other condition excepting acute myeloblastic leukemia, in contrast to which, however, the newly described condition runs a chronic course lasting from three to nine months. Professor Seyderhelm of Frankfurt on the Main, who has provided a full description of the entity, calls it "malignant anemia."

In the foreground of the clinical picture is the severe anemia, which cannot be ameliorated by any hematopoietic agent or by administration of liver. Only by blood transfusions can life be prolonged and then for but a brief while; no remissions in the blood picture are effected thereby, however. The color of the patient is usually straw yellow and reminiscent of the pernicious anemia patient; yet there is no increased destruction of blood cells, no glandular swelling and no enlargement of the spleen. An achylia gastrica is nearly always present. Hemorrhage from the alveolar and nasal mucosa is a common symptom and cutaneous hemorrhage occurs toward the end. There is recurring fever. The course is always fatal. In the leukocyte count there is a predominance of from 70 to 90 per cent of nongranular,

ostensibly lymphoid, cells which are identifiable as myeloblasts by the positive oxydase reaction. The leukocyte count amounts initially to from 3,000 to 5,000; later it is wont to increase to from 10,000 to 15,000 or more (pseudoleukemic myeloblast picture). Microscopic studies disclose a large number of myeloblasts in the marrow, and foci of myeloblasts in the liver and spleen. The splenic pulp is filled with myeloblasts: Periportal and intercapillary foci are present in the liver. The absolute shortage of neutrophils, the absence of thrombocytes in the blood and the high grade anemia suggest a kinship with agranulocytosis and panmyelophthisis. However, there is no question of a proliferation of cells but rather of a disturbed development of the myeloblasts accompanied by secondary decomposition and metaplasia. This was proved by studies made by Seyderhelm and Vollmar, and through tissue cultures of leukocytes obtained from normal blood and blood of myeloid leukemia and "malignant leukemia" patients. Whereas the leukocytes of myeloid leukemia are round cells with abundant protoplasmic flow and exhibit almost no motility, the leukocytes in "malignant anemia" form numerous ameboid processes and show rapid movement, characteristics not to be observed elsewhere except in tissue cultures of sarcoma and carcinoma cells. Microscopic study of the leukocytes discloses the principal difference in the functional condition of particular types of leukocytes; such determinations are impossible by means of a purely morphologic cell count. It has further been established that "malignant anemia" may be transmitted to chickens and rabbits but not to rats and guinea pigs. The affected animals develop a hyperchromic anemia from which they recover in time. In the blood and bone marrow of the more recently observed "malignant anemia" patients, other cellular formations were determined which, in their structure and specific stainability (victoria blue), resembled ultramicroscopic virus. Similar structures have also been found in some of the sick animals. The possibility that this observation is of etiologic significance must for the present be evaluated only most critically and cautiously.

Treatment of Carcinoma of the Cervix Uteri

The ordinaris in gynecology at Koenigsberg recently reported on the therapy of carcinoma of the cervix uteri, in use at the university's gynecologic clinic, which he directs. The statistics submitted cover twenty-seven years (1910-1927); they are of special interest because the well directed Koenigsberg clinic has at all times been particularly concerned with this problem. During the specified period 1,479 women were first treated for carcinoma of the cervix uteri at the clinic. During the directorship of Prof. Georg Winter (1910-1925) complete permanent remissions were obtained in 15 per cent of the cases (in the period from 1910 to 1913) and in 11.5 per cent (in the period 1919-1925). The number of patients who were lost track of by the clinic is, to be sure, around 12 per cent. Besides one should remember that during the mentioned periods radiotherapy, if utilized at all, was still only in its rudimentary stages as a technical procedure. Under Prof. Wilhelm Zangemeister, director from 1926 to 1932, the proportion of complete permanent remissions rose to 18 per cent; surgery had by that time been completely relegated to the background in favor of intensive irradiation. Since 1932, under the present director, "defective" therapy, in Stoekel's sense of the term, has been applied to cancer cases at Koenigsberg, as elsewhere; surgical interventions (radical vaginal operation) were performed on about 33 per cent of the patients. Among women who underwent operations in 1932 and for whom follow-up records of the five ensuing years are extant, the proportion of complete remissions was 30 per cent, the optimal corresponding incidence thus far obtained. In recent years (1932-1936) primary operative mortality amounted to 4.4, primary mortality of patients treated with radium to 3 per cent. Of patients who died within the last five years a larger proportion were kept free of recurrence and capable of activity for more or less substantial periods.

AUSTRALIA

(From Our Regular Correspondent)

Sept. 27, 1938.

Hydatid Disease in New Zealand

The figure for hydatid admissions to public hospitals in New Zealand during 1937 is the second highest on record, 126 compared with a figure of 133 for 1936 (the record) in a population of 1½ million. A fair estimate places the number of fresh cases of infection at from 125 to 150 a year and there is evidence to show that, although in some districts (Otago for example) hydatid disease is less common than it used to be, in New Zealand as a whole the incidence of the disease is increasing rather than diminishing. Christchurch Metropolitan Hospital last year showed a proportion of one hydatid for every 216 patients, a rate heretofore unequaled in New Zealand or in Australia. Mortality figures have apparently decreased. In 1937 fourteen deaths were reported for the whole of the dominion, eight of which occurred in public hospitals.

Figures for the incidence of hydatids in sheep and cattle in New Zealand are high and show no sign of diminution. Stated generally, on an average about half of these farm animals, which are essential to the country's economic welfare, are found infected. In old sheep in some districts the incidence approaches 100 per cent.

The incidence of hydatid tapeworm in dogs is also high. From these figures it is easily seen that opportunities are abundant for dogs to become infected through feeding on raw livers or lungs of sheep containing hydatid cysts. It has been shown that only about one third of New Zealand dogs are susceptible to infection, but there are 150,000 dogs in a population of 1,500,000 human beings.

DEPARTMENT FOR HYDATID RESEARCH

For many years a small but active department at the medical school has been engaged in the work of hydatid disease research and has, among other things, organized and conducted a vigorous campaign of prevention. This year has seen the inauguration by the New Zealand government of a national council for medical research, whose main functions will be to foster the study of the prevention of such menaces to the public welfare as tuberculosis, cancer, goiter, hydatid disease and malnutrition and, when deemed necessary, to provide the funds required. The medical school department for hydatid research will henceforth continue its work as a unit in this organization.

Tables of human incidence compare unfavorably with those regarding prevalence in all other countries except Uruguay and Argentina, where hydatid disease continues to be regarded as a national malady. These two countries, particularly Uruguay, are now organizing an intensive campaign of hydatid prevention largely on the educative and legislative lines which have been adopted in New Zealand.

Ophthalmological Society of Australia

Interest attaches to the recently formed Ophthalmological Society of Australia, chiefly because of its constitutional relationship with the British Medical Association in Australia. In Great Britain and elsewhere it is customary for independent clinical societies to be formed or to exist outside the British Medical Association. Such a tradition bears inherent weaknesses, for such small independent societies can rarely unite for common action. In Australia the members of the British Medical Association have made a new departure. The ophthalmologists of the commonwealth felt that they needed a society in which those practicing this branch of medicine could unite for the advancement of their specialty by meetings, publications, libraries and museums, research work and the provision of prizes for research work, and by postgraduate lectures. Instead of starting an independent body they have formed such a society within the association—the Ophthalmological Society of

Australia (British Medical Association). Those eligible for ordinary membership are all those members of the British Medical Association who specialize in ophthalmology and whose qualifications are approved by the council of the society. Its rules show that it is completely autonomous yet part of the association. It is hoped that the successful functioning of this society may induce some of the existing extramural bodies to become part and parcel of the British Medical Association and in so doing consolidate the unity of the profession, for unity among medical men was never so essential as now, when medicine is threatened with state control, which, unless much opposition is presented, is certain to develop along empirical rather than scientific lines.

Fatal Injections of Paraldehyde

There occurred in Sydney recently the death of two brothers, aged 15 and 13, following rectal injections of paraldehyde given them at a private hospital preparatory to an operation for the removal of tonsils. Postmortem examinations established the cause of death in each case as asphyxia with cardiac failure due to an overdose of the drug. It was disclosed at the inquest that the material for injection had been dispensed as ounces instead of drachms. Although every possible treatment was used in an endeavor to save the boys' lives after the discovery of the mistake, both died within twenty-four hours of the injection. The chemist responsible was committed for trial on a charge of manslaughter. Evidence was given for the defense that he possessed an excellent record as a chemist and that except for this fatal error he was a careful and efficient dispenser. He had, however, been through severe treatment for cancer of the throat, which apparently had now been cured. It was contended that in this condition of suffering even a skilled man might easily make a mistake. He was employed at a Friendly Society dispensary and dealt with between 800 and 1,000 prescriptions a month. At the time of the fatal mistake he was making them up at the rate of one every minute and a half. The jury returned a verdict of not guilty. It was pointed out, however, that negligence on the part of a dispenser is a very grave menace to the public and therefore is criminal negligence.

Marriages

THOMAS J. FLOYD JR., Jersey City, N. J., to Miss Juliette Jordan of Eufaula, Ala., in Columbus, Ga., in August.

RAYMOND STEADMAN, Kingsport, Tenn., to Miss Bonnie Day of Little Rock, Ark., at Franklin, Tenn., September 3.

WILLIAM STURGES PARKER, Merion Station, Pa., to Miss Anita Woodruff Jones of Philadelphia, September 10.

JOSEPH E. FUNK, Laurelton, N. Y., to Miss Margaret Christopher of Perth Amboy, N. J., August 20.

ROBERT GORDON CARNAHAN to Miss Sara Elisabeth Alexander, both of San Antonio, Texas, September 8.

CHARLES LEE BUXTON, New York, to Miss Helen Morgan Rotch of Middleboro, Mass., September 3.

MAURICE F. STOCK, Fresno, Calif., to Miss Angela Blanche Schlich of Okawville, Ill., September 22.

ALFRED M. PAISLEY, Jacksonville, Ill., to Miss Elizabeth Winger of Keokuk, Iowa, September 3.

ALBERT P. D'ERRICO, Dallas, Texas, to Miss Carol Whitney Van Etten of New York, October 18.

THOMAS HARROP MILLER to Miss Mary Katherine Flinterman, both of Detroit, September 10.

JOSIAH CHARLES TRENT, Okmulgee, Okla., to Miss Mary Duke Biddle of New York in June.

HERBERT F. LARAMORE, Livingston, Texas, to Miss Jean Howell of Atlanta, Ga., August 29.

JESSE JAMES PORTER, Norton, Va., to Miss Nell Campbell of Princeton, W. Va., September 10.

MAURICE ERVIN HODGSON to Miss Bettie Fullerton Marshall, both of Pittsburgh, July 20.

Deaths

Earl Baldwin McKinley ☉ dean and professor of bacteriology at the George Washington University School of Medicine, Washington, D. C., was on the *Hawaii Clipper* which was lost over the Pacific Ocean en route to Manila July 28. Dr. McKinley was born in Emporia, Kan., Sept. 28, 1894. He received a degree from the medical school of the University of Michigan, Ann Arbor, in 1922, where he was instructor of bacteriology and biochemistry during 1919 and 1922. During 1924 and 1925 he was a fellow of the National Research Council and studied at the Pasteur Institute of the University of Brussels. In 1922 he was appointed assistant professor of pathology and bacteriology at Baylor University College of Medicine, Dallas, Texas, and in 1923 was made professor of hygiene and bacteriology and chairman of the department. In 1925 and 1926 he was assistant professor of bacteriology at the Columbia University College of Physicians and Surgeons, New York, and in 1926 and 1927 was an associate professor. He was professor of bacteriology at the same school and director of the School of Tropical Medicine, University of Puerto Rico, from 1928 to 1931. During 1927-1928 he was field director of the International Health Board at Manila, P. I. He was an intelligence officer of the U. S. Army during the World War. Dr. McKinley was a fellow of the American College of Physicians and the Royal Society of Tropical Medicine and Hygiene (London); corresponding member of the Société belge de médecine tropicale (Brussels); in 1938 president and in 1936-1937 vice president, American Association of Pathologists and Bacteriologists; formerly secretary of the American Academy of Tropical Medicine; member of the executive committee, division of medical sciences of the National Research Council; member and on the editorial boards of the Society of American Bacteriologists and the American Association of Immunologists. He was secretary and member of the advisory board of the American Leprosy Foundation and executive secretary and director of the American Foundation for Tropical Medicine. Dr. McKinley was the author of "Filterable Virus Rickettsia Diseases," 1929, and "A Geography of Disease," 1935.

Archie Burt Chappell ☉ Middletown, N. Y.; Albany (N. Y.) Medical College, 1905; member of the American Academy of Pediatrics; past president of the Orange County Medical Society; member of the board of health; on the staffs of the Horton Memorial Hospital, Middletown, Newton (N. J.) Memorial Hospital, Goshen (N. Y.) Hospital, Monticello (N. Y.) Hospital, Tuxedo Memorial Hospital, Tuxedo Park, Maimonides Hospital, Liberty, and the Municipal Sanatorium, Otisville; aged 55; died, August 28, of coronary occlusion.

Harold Merle Goodwin, Bangor, Maine; Harvard University Medical School, Boston, 1913; past president of the Penobscot County Medical Society; member of the Maine Medical Association; fellow of the American College of Surgeons; served during the World War; on the staff of the Eastern Maine General Hospital; aged 52; died, August 10, of adenocarcinoma of the cecum with secondary involvement of the liver.

Leo Howard Flynn, Eau Claire, Wis.; Northwestern University Medical School, Chicago, 1912; member of the State Medical Society of Wisconsin; past president and secretary of the Eau Claire County Medical Society; city physician, county physician and city health officer; served during the World War; on the staffs of the Sacred Heart and Lutheran hospitals; aged 54; died, August 19, of coronary occlusion.

Lowell Mason Gates, Scranton, Pa.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1878; member of the House of Delegates of the American Medical Association in 1913 and 1915; member and formerly vice president of the Medical Society of the State of Pennsylvania; past president of the Lackawanna County Medical Society; aged 86; died, August 14.

Anders G. Hovde ☉ Los Angeles; University of Minnesota College of Medicine and Surgery, Minneapolis, 1903; member of the American Academy of Ophthalmology and Oto-Laryngology; fellow of the American College of Surgeons; on the staffs of the Hollywood Hospital and the Queen of Angels Hospital; aged 62; died, August 14, of coronary thrombosis.

Adolphus George Wippert, Chicago; Missouri Medical College, St. Louis, 1890; College of Physicians and Surgeons, Medical Department of Columbia College, New York, 1892; member of the Illinois State Medical Society; formerly on the staff of St. Elizabeth's Hospital; aged 70; died, August 15, of arteriosclerosis, nephritis and diabetes mellitus.

Frank C. Richmond, Madison, Wis.; College of Physicians and Surgeons of Chicago, 1894; member of the American Orthopsychiatric Association; formerly director of the psychiatric field service of the Wisconsin State Board of Control; formerly a lawyer; aged 64; died, August 29, in St. Mary's Hospital, of coronary thrombosis.

Clarence A. Earle ☉ Des Plaines, Ill.; College of Physicians and Surgeons of Chicago, 1887; member of the American Academy of Pediatrics; for many years attending physician to St. Mary's Training School; on the staff of the Northwestern Hospital; aged 76; died, October 28, in St. Luke's Hospital, Chicago, of coronary thrombosis.

William Madison Higgins, New York; University of Vermont College of Medicine, Burlington, 1909; formerly instructor and lecturer in gynecology at the University and Bellevue Hospital Medical College; fellow of the American College of Surgeons; aged 57; on the staff of the Bellevue Hospital, where he died, August 20.

William Anderson ☉ Sharpsburg, Pa.; Western Pennsylvania Medical College, Pittsburgh, 1900; served during the World War; on the staff of the Western Pennsylvania Hospital, Pittsburgh; aged 66; died, August 14, in the Woman's Christian Association Hospital, Jamestown, N. Y., of coronary thrombosis.

George Hall Beers, Auburn, N. Y.; College of Physicians and Surgeons, Medical Department of Columbia College, New York, 1891; on the staffs of the Auburn City and Mercy hospitals; past president and secretary of the Cayuga County Medical Society; aged 69; died, August 16, of coronary thrombosis.

Hiram Benjamin Martin, Huntington, W. Va.; Eclectic Medical Institute, Cincinnati, 1905; member of the West Virginia State Medical Association; served during the World War; aged 57; on the staff of St. Mary's Hospital, where he died, August 23, of uremia and cardiorenal vascular disease.

Charles Ralston Hughes ☉ Philadelphia; Medico-Chirurgical College of Philadelphia, 1911; served during the World War; on the staff of the Bryn Mawr (Pa.) Hospital; aged 51; died, August 10, of *Streptococcus viridans* septicemia with sub-acute bacterial endocarditis.

James Robert Nelson, Kingston, N. Y.; College of Physicians and Surgeons, Medical Department of Columbia College, New York, 1869; on the staff of the Kingston Hospital; aged 90; died, August 24, of cerebral hemorrhage and arteriosclerosis.

Albert Prentiss Alexander, Como, Miss.; Memphis (Tenn.) Hospital Medical College, 1903; member of the Mississippi State Medical Association; county health officer; for many years president of the school board; aged 63; died, August 9.

Edward Alexander Wareham ☉ Hagerstown, Md.; University of Maryland School of Medicine, Baltimore, 1883; on the staff of the Washington County Hospital; aged 79; died, August 18, of carcinoma of the prostate with metastases to the bladder.

Horace Maurice Mayfield, Tyler, Texas; University of Texas School of Medicine, Galveston, 1932; on the staff of the Mother Francis Hospital; aged 31; died, August 25, of anaphylactic reaction due to the bite of an insect, presumably the red wasp.

Elias Wyman Davis, Seymour, Conn.; Yale University School of Medicine, New Haven, 1892; past president of the New Haven County Medical Society; aged 84; died, August 30, in Hartford of fracture of the neck of the femur and pneumonia.

Charles Dunaway Quinn, Utica, N. Y.; Columbia University College of Physicians and Surgeons, New York, 1921; on the staff of St. Luke's Home and Hospital; aged 40; died, August 26, of acute appendicitis, tuberculosis and peritonitis.

Harrison Gray ☉ Norwich, Conn.; Jefferson Medical College of Philadelphia, 1919; health officer; served during the World War; on the staff of the William W. Backus Hospital; aged 61; died, August 26, of coronary thrombosis.

Edward Broquet, New York; College of Physicians and Surgeons, Medical Department of Columbia College, New York, 1886; member of the Medical Society of the State of New York; aged 80; died, August 4.

Clarence Mangan Malone, Shamokin, Pa.; Medico-Chirurgical College of Philadelphia, 1898; served during the World War; aged 61; died, August 9, at the Shamokin State Hospital of cerebral hemorrhage.

William George Scott, Portland, Ore.; St. Louis University School of Medicine, 1911; served during the World War; aged 56; died, August 27, of coronary thrombosis, uremia and polycystic kidneys.

Arthur L. Seyse ☉ Arcade, N. Y.; University of Buffalo School of Medicine, 1908; for many years health officer and formerly coroner; aged 55; died, August 29, of cerebral hemorrhage and heart disease.

Norbert Julius Lowry, Cresco, Iowa; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1902; aged 59; died, August 31, of coronary thrombosis.

Robert McGeehon Hope, Mereer, Pa.; Cincinnati College of Medicine and Surgery, 1874; member of the Medical Society of the State of Pennsylvania; aged 89; died, August 3, at New Wilmington.

Frank Harvey Grim, Revere, Pa.; Jefferson Medical College of Philadelphia, 1881; for many years director of the township schools and formerly secretary; aged 78; died, August 16.

John Henry Steidl, Trudeau, N. Y.; Harvard University Medical School, Boston, 1929; assistant superintendent of the Trudeau Sanatorium; aged 39; died, August 9, of uremia.

John R. Langford, Swansea, S. C.; College of Physicians and Surgeons, Baltimore, 1885; member of the South Carolina Medical Association; aged 82; died, August 21, at Pelion.

Albert George Mott, Bellerose, N. Y.; New York Homeopathic Medical College and Flower Hospital, New York, 1912; aged 50; was killed August 6, in an automobile accident.

Robert Richard Wallace, Hamilton, Ont., Canada; University of Toronto Faculty of Medicine, Toronto, 1882; L.R.C.S., L.R.C.P., Edinburgh, Scotland, 1882; died, August 15.

William J. A. O'Hara ☉ Bridgeport, Conn.; College of Physicians and Surgeons, Baltimore, 1893; aged 74; died, August 4, of hypertensive heart disease and hemiplegia.

Edwin Ewell Harris, Grinnell, Iowa; Howard University College of Medicine, Washington, D. C., 1895; member of the Iowa State Medical Society; aged 71; died, August 6.

Edward J. Douhet, Lakewood, Ohio; Western Reserve University Medical Department, Cleveland, 1885; aged 72; died, August 4, in the Fairview Park Hospital, Cleveland.

Jerome C. McKinley, York, Neb.; Louisville (Ky.) Medical College, 1891; aged 77; died, August 7, in a sanatorium at Lincoln of cerebral hemorrhage and arteriosclerosis.

Vasilios Konstantinos Papavasiliou, Boston; Tufts College Medical School, Boston, 1915; member of the Massachusetts Medical Society; aged 54; died, August 1.

Thomas Harrison Mitchell, Jamestown, Pa.; Bellevue Hospital Medical College, New York, 1872; aged 88; died, August 2, of a fractured femur received in a fall.

Hugo Kunz, New York; Bellevue Hospital Medical College, New York, 1893; member of the Medical Society of the State of Pennsylvania; aged 68; died, August 8.

William Fay Ross ☉ Aspinwall, Pa.; Jefferson Medical College of Philadelphia, 1905; served during the World War; aged 57; died, August 16, of coronary occlusion.

Frederick Lincoln Clark, New Bedford, Mass.; Boston University School of Medicine, 1888; aged 73; died, August 30, in South Dartmouth of pulmonary tuberculosis.

William Owen Lawrence, Leeds, Ala.; Birmingham Medical College, 1909; member of the Medical Association of the State of Alabama; aged 53; died, August 4.

Cephas Z. Wingerd, Sharpsburg, Md.; Jefferson Medical College of Philadelphia, 1874; aged 88; died, August 11, of cerebral hemorrhage and arteriosclerosis.

O. Eugene Larkin, Milton, Wis.; Chicago Medical College, 1884; member of the Illinois State Medical Society; aged 83; died, August 12, of coronary embolism.

Ashbel Fairchild Ruble, Wheeling, W. Va.; Eclectic Medical Institute, Cincinnati, 1894; aged 70; died, August 16, in the Ohio Valley General Hospital.

Sara Allen Castle, Meridian, Miss.; Woman's Medical College of Baltimore, 1900; Cornell University Medical College, New York, 1901; died, August 22.

Albert Edward Brown, Webster, S. D.; American College of Medicine and Surgery, Chicago, 1905; aged 75; died, August 4, of cerebral hemorrhage.

Edwin Augustine Swan, St. Petersburg, Fla.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1875; aged 83; died, August 15.

Benjamin Edward Selman, Silsbee, Texas; Memphis (Tenn.) Hospital Medical College, 1890; formerly county health officer; died in August.

Albert Douglas Miller, Humboldt, Iowa; State University of Iowa College of Medicine, Iowa City, 1912; aged 50, died, August 20, of heart disease.

Antonio de Robertis, Boston; Regia Università di Napoli Facoltà di Medicina e Chirurgia, Italy, 1892; aged 69; died, August 23, of myocarditis.

George Leonard Wagner, Deshler, Neb.; Cotner University Medical Department, Lincoln, 1914; aged 54; died, August 15, of myocarditis.

Nahum Kavinoky, Los Angeles; University of St. Vladimir Faculty of Medicine, Kiev, Russia, 1898; aged 62; died, August 4, of heart disease.

Eleanor I. Horn Parsons, Lake George, N. Y.; Bennett Medical College, Chicago, 1885; aged 75; died, August 17, of carcinoma of the bladder.

James Copeland Gibson, Jacksonville, Fla.; Queen's University Faculty of Medicine, Kingston, Ont., Canada, 1896; aged 56; died, August 28.

Mary E. Donaldson Dennis, Los Angeles; University of Southern California College of Medicine, Los Angeles, 1897; aged 68; died, August 27.

William E. Pittman, Roseville, Ill.; Rush Medical College, Chicago, 1885; member of the Illinois State Medical Society; aged 79; died, August 8.

Richard S. Wilson, Willshire, Ohio; Fort Wayne (Ind.) College of Medicine, 1891; aged 82; died, August 14, of carcinoma of the stomach.

Elizabeth Bartos ☉ Cleveland; Western Reserve University Medical Department, Cleveland, 1924; aged 39; died, August 14, in Albany, N. Y.

Merritt Meade Hill, Elverton, W. Va.; Medical College of Virginia, Richmond, 1925; aged 37; died, August 31, of an overdose of a drug.

Isaac P. Poynor, Houston, Texas (licensed in Texas, under the Act of 1907); veteran of the Spanish-American War; aged 71; died, August 7.

Harry Y. Hartman, Orwigsburg, Pa.; Jefferson Medical College of Philadelphia, 1880; aged 81; died, August 18, of bronchopneumonia.

Bliss Adam Marven, Moncton, N. B., Canada; University of Vermont College of Medicine, Burlington, 1886; aged 76; died, August 22.

Nathan Absalom Arrants, Decatur, Tenn.; Vanderbilt University School of Medicine, Nashville, 1885; aged 81; died, September 24.

Joseph Salmon Marblestone, New York; University and Bellevue Hospital Medical College, New York, 1906; died, August 20.

Sarah Elizabeth Winter, Media, Pa.; Woman's Medical College of Pennsylvania, Philadelphia, 1892; aged 69; died, August 22.

Elmer Julius Boeseke, Santa Barbara, Calif.; Chicago Medical College, 1889; formerly mayor; aged 70; died, August 25.

Herbert W. Allen, Glendale, Calif.; University of the City of New York Medical Department, 1883; aged 76; died, August 18.

William Shira, La Rue, Ohio; Bellevue Hospital Medical College, New York, 1877; aged 92; died, August 17, in Edgewood, Pa.

Robert H. Morrell MacKenzie, Pittsburgh; Baltimore University School of Medicine, 1898; aged 69; died, August 15.

Thomas M. Stapleton ☉ Chicago Heights, Ill.; Chicago College of Medicine and Surgery, 1914; aged 53; died, August 9.

Eugene H. McCullers, Clayton, N. C.; Bellevue Hospital Medical College, New York, 1888; aged 74; died, August 14.

Fredrick Leonidas Smith, Eufaula, Okla. (licensed in Oklahoma under the Act of 1908); aged 70; died, August 22.

J. W. De Noon, Cedar Rapids, Iowa (licensed in Iowa in 1886); aged 86; died, August 7, of carcinoma of the cecum.

Thomas Oscar Young, Princess Anne, Md.; Jefferson Medical College of Philadelphia, 1880; died, August 3.

Mark Elbaum, Milwaukee; Rush Medical College, Chicago, 1937; aged 28; died, August 15, of tuberculosis.

Edward Plews Kermott, Glendale, Calif.; Rush Medical College, Chicago, 1889; aged 77; died, August 8.

Milton S. Kuhn, Mount Pleasant, Pa. (licensed in Pennsylvania in 1901); aged 81; died, August 14.

Correspondence

"COLD VACCINES"

To the Editor:—Referring to the article "Cold Vaccines: An Evaluation Based On a Controlled Study," in *THE JOURNAL*, September 24, may I point out certain defects in an evaluation based on the statistics gathered as reported?

1. The employment of respiratory group bacterial vaccines—loosely termed "cold vaccines"—for the purpose of protecting against the widely varying and innumerable primary causes of lesions of the respiratory mucosa does not accord with the immunologic principles involved.

2. The "stepping up in virulence," with increasing morbidity rates and with increasing mortality rates, due to bacterial diseases that are nearly always sequels to the milder respiratory disorders, is not considered in the evaluation—more particularly a virulence during the rapid spread of epidemic coryza and influenza.

3. The statement that "few studies of these vaccines have been adequately controlled" fails to consider the evidence, identical in large part, with statistics on pneumonia. For example: 1. Reports from the Commission on Pneumonia appointed by the Surgeon General of the U. S. Army during the apallingly fatal epidemic of 1918—statistics which were incorporated in the general order for vaccination of the entire troops. 2. The campaign to reduce the death rate of pneumonia in New York State, with the objects of reducing the incidence of pneumonia and of providing better treatment for patients, published in the Year Book of General Medicine, 1936, pages 184-185, for statistics by Felton, and pages 184-199 for evaluations by Cecil, Case and others.

G. H. FONDÉ, M.D., Mobile, Ala.

HUMAN REQUIREMENTS FOR VITAMIN B₁

To the Editor:—All those who are seeking to clarify the position with regard to human requirements for vitamin B₁ will appreciate Dr. Cowgill's timely and comprehensive summary.

Recent work from all quarters has tended to confirm Dr. Cowgill's original suggestion of 300 international units as a basal protective level for an "average man" weighing 70 Kg. who consumes 3,000 calories a day, and it would seem clear that additions to this must be expected for normal good health and in all conditions in which there is increased metabolism.

The 1935 publication of the Technical Commission of the League of Nations Health Committee, in which from 150 to 250 international units of vitamin B₁ was recommended as the requirement for pregnancy and lactation, naturally obtained widespread publicity, and Dr. Cowgill rightly points out that "such a recommendation seems altogether too low." The commission's attention has frequently been called to this fact, emphasis being laid on two points: first, that diets of such levels have been associated with beriberi, and, second, that the diets actually recommended by the commission do, in fact, contain considerably more vitamin B₁ than these figures represent.

It is noteworthy that in the most recent publication of the commission (June 1938) the recommendation has been altered as follows:

"Vitamin B₁.—As a result of considerable experience, an allowance of 10 international units per 100 calories of food-intake seems to be adequate. This allowance would place at 300 international units the daily requirement for an adult of 70 kilogrammes body-weight receiving a diet of 3,000 calories.

"The above estimate has been confirmed by consideration of the vitamin B₁ content of a large number of diets which protected human beings from vitamin B₁ deficiency, in contrast to others which did not provide such protection.

"The requirements of animals for vitamin B₁ have been shown experimentally to be greatly increased during pregnancy and lactation. Pending direct evidence, it is recommended that the

diets of pregnant and lactating women should contain 2 to 3 times the minimum allowance for the adult in general. The quantities of vitamin B₁ recommended above would probably be contained in ordinary mixed diets when lightly milled cereals are a staple of the diet, or when milk, fruits and vegetables are freely used and highly milled cereals and sugars are not allowed to displace protective foods.

"The requirements of the infant for vitamin B₁ would appear to be met by about 10-15 international units per 100 calories of food-intake. An allowance of 200-250 international units daily is probably sufficient for nursery school-children."

Thus the minimum protective level suggested is now brought up to Dr. Cowgill's 300 unit level, and the quantities suggested for pregnant and lactating women are at least from 600 to 900 units. This would seem to be more nearly in line with the experimental and clinical data at present available.

AUDREY Z. BAKER, B.Sc., M.R.C.S., L.R.C.P.,
London, England.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

MEDICINAL BATHS

To the Editor:—I should like to have an opinion on therapy of medical baths as practiced in Europe. Foreign physicians have apparently brought with them into this country the idea of medicinal baths; for example, the carbonic acid bath, the oxygen bath, the oxygen bath with iodide. I do not mean the natural spring baths so much as I mean the packaged chemicals which are used in a patient's home. Please discuss this subject.

M.D., New York.

ANSWER.—The exact sphere of usefulness of artificial baths modeled after natural therapeutic baths has not been determined. It would seem in many instances that medicinal baths play only a minor role in the therapeutic regimen of the spa. At the spa, change of environment, regulation of activities, modification of diet, change of climate and institution of therapeutic measures may all be factors in the beneficial effects which are obtained. When one attempts to reproduce the beneficial effects of spa treatment simply by adding certain chemicals to the water in the patient's own bathtub, little benefit results.

There are some physicians, however, who feel that artificial Nauheim baths may be of some value in the management of certain milder forms of cardiac decompensation. The so-called "Sprudel" water of Bad Nauheim is a naturally warm, saline solution, highly impregnated with carbonic acid gas. The temperature varies from 86 to 93 F. One may add 32 ounces of sodium bicarbonate and 22 ounces of sodium acid sulfate to 40 gallons of warm water (86 to 93 F.) to produce an artificial Nauheim bath which will generate approximately 250 cc. of gas per liter of water. Any competent pharmacist can supply the physician with a formula for the chemicals to be used in preparing such a bath.

Though there is little information available on "oxygen" baths, there are certain natural waters in Europe which contain iodides and bromides. For example, the water at Woodhall spa in Lincolnshire, England contains 7.68 mg. of potassium iodide and 50 mg. of potassium bromide per liter. Iodides and bromides are present in minute quantities in many "muriated" waters. Such baths could be produced artificially but there is so little evidence that these substances in minute quantities are of value that there seems no reason to add them.

It is unquestionably true that American physicians have paid insufficient attention to their own natural spas and that they are not nearly as conscious of the value of spa therapy as are European physicians. Nevertheless, the attempt to produce artificial mineral waters for use in the patient's home seems a dubious procedure at the very best. Because the skin is incapable of any great amount of absorption, medicinal agents incorporated in baths produce little or no therapeutic effect. One may therefore conclude that, while the natural spa regimen may be of considerable value in the management of certain diseases, due essentially to environmental conditions, artificial medicinal baths, for home use, on the other hand, have an extremely limited field of usefulness.

PEPTIC ULCER AND SERORESISTANT SYPHILIS

To the Editor:—A white man aged 49 has a peptic ulcer, the diagnosis having been confirmed by x-ray examination. A routine blood Wassermann reaction was 4 plus. This was rechecked and the Wassermann, Kline, Kahn and Hinton reactions were all 4 plus. Antisyphilitic therapy was started March 22, 1938, and until May 20 the patient received ten weekly injections of bismuth in oil 1 Gm. and eight weekly injections of nearsphenamine 4.05 Gm.. A blood Wassermann reaction May 27 was still 4 plus. From June 1 to August 2 the patient again received ten injections of bismuth in oil 1 Gm. and eight injections of nearsphenamine 4.5 Gm. The blood Wassermann reaction August 6 was again 4 plus. The patient has been feeling fine and cannot recall when he became infected. A spinal tap has not been done yet. Can I give him a rest or shall I continue with the weekly injections of bismuth in oil and nearsphenamine? Is it advisable to change to a soluble bismuth salt and to another arsenical, such as mapharsen? Is there any possibility of bringing the blood Wassermann reaction to negative with future treatment or is this case liable to turn out to be a Wassermann fast case because of the lack of early treatment? M.D., New York.

ANSWER.—As pointed out by Parsons, Plummer and Gaskill in *THE JOURNAL* June 11, 1938, page 1991, there is a high degree of frequency of association between peptic ulcer and syphilis of the central nervous system. In any patient with long-standing syphilitic infection, however, even in the absence of this association and even in the absence of obvious neurologic evidences of syphilis of the central nervous system, it is essential to test the spinal fluid as early as possible in the course of treatment in order to direct treatment intelligently. The character and amount of further treatment cannot be determined in the patient in question without this information. It is therefore undesirable to give him a rest period at the present time, but instead the spinal fluid should be tested promptly.

Whether weekly injections of a bismuth compound and nearsphenamine should be continued or whether, on the contrary, the patient should now be treated with fever therapy, tryparsamide or both, or with some other trivalent arsenical drug, cannot be stated without information as to the spinal fluid reaction.

The possibility of reversal of the blood Wassermann reaction to negative cannot be definitely stated as to this particular patient. In general terms from 35 to 50 per cent or more of all patients with late syphilis are seroresistant under any form of antisyphilitic treatment. The relative importance of serologic reversal to the other aims of the treatment of late syphilis should, however, be kept in mind. In any patient with late syphilis the aims of treatment are four: 1. If lesions of syphilis are present or if the patient has symptoms attributable to syphilitic infection, treatment is planned to heal the lesions or to relieve the symptoms. 2. Treatment is continued past the point of symptomatic relief in order to prevent the development of progression or relapse in the future. 3. If no lesions or symptoms are present at the initiation of treatment, the entire course of treatment is planned as prophylaxis for the future for the prevention of progression or relapse. 4. The least important element of the treatment of late syphilis is serologic reversal.

In connection with the problem of Wassermann fastness the inquirer should read the article by J. E. Moore and Paul Padgett, *The Problem of Seroresistant Syphilis*, *THE JOURNAL*, Jan. 8, 1938, page 96.

DIET OF MOTHER DURING LACTATION

To the Editor:—There has been much discussion as to the foods nursing mothers can and cannot eat because of the effect on the baby. I have been unable to find any definite literature on this subject and should like to have a list of the foods which a nursing mother should not eat because of producing ill effects on the baby, such as colic.

M.D., Nebraska.

ANSWER.—For the average mother and the average baby there are no foods which need to be deleted from the diet because of producing ill effects on the baby such as colic. A mother may eat anything that agrees with her own digestion. A diet which is suitable for her under normal conditions will be suitable during the period of lactation except that she will need to take a somewhat larger amount. The mother's diet must be well balanced and must contain foods rich in vitamins such as milk, butter, eggs, leafy green vegetables and raw fruits. There seems to be no good basis for the idea that the nursing mother cannot take acid fruits, vegetables or salads. These are all good for her if they do not upset her digestion. There is no evidence that the taking of moderate amounts of alcoholic beverages, or of tea and coffee or smoking in moderation affects the character of the milk adversely, provided the mother herself is not affected. Occasionally highly spiced foods and condiments such as mustard, red pepper, vinegar, pickles and pepper soups may seem to cause distress in the infant. Also occasionally such foods as garlic, onions or asparagus, which give a distinct odor or taste to the milk, may cause infants to object.

Occasionally also an infant may be allergic to one or more foods in the mother's diet, resulting in allergic manifestations in the infant. Certain laxatives taken by the mother may cause loose stools in the infant, as may certain laxative fruits. Cause and effect is the best way to determine the relation of a food to distress or colic in the baby. If the condition in the infant clears up when the food is eliminated from the mother's diet, that is proof. However, this rarely happens and it is doubtful outside of allergic infants whether a well rounded mother's diet has any deleterious influence on the nursing infant.

TREATED MOTHER AND CONGENITAL SYPHILIS—
DANGER TO OBSTETRICIAN

To the Editor:—A woman, eight months pregnant, has syphilis. Her Wassermann reaction is still 4 plus. She has been given the routine bismuth, nearsphenamine and mercury treatment since she was two and one-half months pregnant. Is there any possibility of the baby's having the disease? Is there any possibility of the obstetrician's contracting the disease if some blood or fluid should be squirted in the mouth or on an abrasion of the skin? How reliable is the Wassermann test during pregnancy?

M.D., Minnesota.

ANSWER.—According to various reports in the literature there is a chance that from 2 to 10 per cent of the children of women with syphilis who have been well treated throughout the pregnancy will manifest congenital syphilis. The amount and intensity of the treatment, the number and extent of the rest periods, and the time in the pregnancy at which treatment was instituted are factors which determine whether or not the child becomes infected. The likelihood that an obstetrician will become infected from blood or amniotic fluid of a patient of this type with syphilis, even though his skin is abraded, is remote. The reason for this may be summarized briefly as follows: The amount of treatment she has received would render her noninfectious, and latent syphilis is but slightly if at all infectious even when not treated. A properly done serologic test is just as reliable in a pregnant woman as in other patients with syphilis. Pregnancy does not produce falsely positive serologic reports if the serologic technic is efficient.

DERMATITIS FROM CEMENT

To the Editor:—Several of my patients have been employed unloading cement for years without any ill effects, but lately they have been unloading a different type of cement, which the laborer tells me is hot. These patients get a severe dermatitis of the arms and legs or any place where the cement touches them. The dermatitis starts with an erythema and an induration of the skin with pain and burning, followed by ulcerations. It is also irritating to the lungs. One of the patients came to have a severe bronchial pneumonia following the unloading of a carload of this cement. The cement is put out by the Universal-Atlas Cement Company, 208 South LaSalle Street, Chicago. Would you kindly inform me what the irritative factor in this cement would be?

M.D., Minnesota.

ANSWER.—The principal raw materials used in the manufacture of hydraulic cement are limestone, chalk, shell, rock cement, clay, shale, bauxite and blast furnace slag. To these materials are added lime, if it is desired to have a quick hardening cement, or gypsum, if a slow hardening cement is desired.

The hygroscopic properties and the alkaline content of cement are the chief causes of its irritant action on the skin, although the grains of silica which it contains may also irritate the skin. When cement comes in contact with water or perspiration, the lime which it contains is slaked, generating heat and forming calcium hydroxide. The withdrawal of moisture from the skin and the resultant heat formation constitute the principal mechanism by which it causes dermatitis, although the calcium hydroxide formed by this reaction and the calcium silicate naturally contained in the cement also play a part in causing dermatitis by acting as solvents for the keratin of the skin. Long exposure to cement, even when the skin is comparatively free from moisture, will cause it to become dry, hard and thick. Such skin is likely to crack and fissure, and indolent ulcers may occur. Workers who perspire freely are more likely to acquire dermatitis from cement than those who do not. For this reason, dermatitis among cement workers is more common in hot weather than in cold. Cement also causes ulcers of the nasal and buccal mucous membranes.

Tomé Bona and Janvier in their article "A Contribution to the Study of Dermatoses of Cement" (*Budapest Sitzungsber.* 13:21, 1935) describe three types of skin lesions caused by cement: The first type consists of vesicles and pustules with edema on the hands and fingers and other exposed parts of the body; the second type consists of softening and thinning of the epidermis resulting in painful swellings, and the third type is hyperemia and folliculitis which usually occurs on the back and upper thorax of workers who carry bags of cement on

their backs. They also describe lesions of the upper respiratory mucous membranes, especially the occurrence of ulcers of the mucous membranes of the cheeks.

The prevention of dermatitis among workers in cement manufacture consists essentially in dust control and cleanliness of the workers. Modern totally enclosed machinery and modern methods of ventilation with local suction vents over dusty processes, compulsory shower baths after work, and the daily change to clean work clothes are preventive measures to be observed in cement factories. The eyes can be protected by wearing goggles and by bathing them in a boric acid solution after work. The mucous membranes of the nose and throat can be protected by respirators. A mild boric acid ointment with a hydrous wool fat base can be inserted into the nostrils to prevent ulceration of the nasal septum. Concrete mixers and those required to unload cement should wear coveralls made of some material impervious to dust as well.

Various protective ointments may be smeared on the skin which may also aid in the prevention of dermatitis from cement. Plain talcum powder dusted on the skin from a convenient container before beginning work has also been found to prevent lime dermatitis.

Treatment of dermatitis among cement workers consists in taking the man off the job and applying mild palliative lotions or ointments until he recovers. Such workers who develop recurrent attacks on resuming work, or who have chronic eczemas, should be transferred to some other occupation.

There is no reason to believe that the cement put out by the Universal-Atlas Cement Company, 208 South LaSalle Street, Chicago, is materially different from other cements. It may be that the cement which the workers now handle and which causes dermatitis is a quick-setting cement and contains more lime than the cement they formerly handled, or it may be that the workers affected have become sensitized to lime, or that the dermatitis occurred at a time when the workers were perspiring more freely than usual.

NEUROSYPHILIS—ANAL CONDYLOMAS

To the Editor:—1. A man aged 48 was diagnosed at a hospital as having meningovascular syphilis. The blood Wassermann reaction was positive (75 per cent fixation), Kahn 4 plus and Rytz positive. Spinal fluid examination showed a slight increase in the amount of globulin, Wassermann test 100 per cent fixation in dilutions of 0.2, 0.4, 0.5 and 1 cc., and cell count 17 per cubic millimeter. He has been given fifteen weekly doses of tryparsamide 3 Gm. and bismuth salicylate in oil 0.13 Gm.; also he has been taking potassium iodide 2 Gm. daily by mouth. What are your suggestions for subsequent treatment? If placed on a routine alternating course of a bismuth compound and mapharsen, can this be instituted without a rest period? 2. A man aged 19 has moist condylomas on the anal region. He gives no history of chancre or secondary eruption. The Kahn test was 4 plus and the Laughlin agglutination test was strongly positive. He was given eight injections of mapharsen 0.06 Gm., followed by ten injections of bismuth salicylate in oil 0.13 Gm. This has been followed by two injections of mapharsen, the first 0.06 and the second 0.04 Gm. He reports chills, nausea and vomiting about two hours after these last two injections. Apparently he has acquired an intolerance to arsenic. What would be your suggested course of treatment? A blood test was taken at the time of the last injection of mapharsen; the report was Kahn and Laughlin reactions negative. The condylomas have not decreased in size or number with this amount of antisyphilitic treatment. Is there any other treatment of the condylomas? Would cauterization of them be advisable? As these lesions are still moist, because of their location would the patient's condition be considered contagious? Would a spinal fluid test be indicated in this case and at what time during the course of treatment?

M.D., Wyoming.

ANSWER.—1. The omission of signs and symptoms of neurosyphilis from the inquiry makes it impossible to classify the type of neurosyphilis. If the clinical manifestations indicate that involvement of the central nervous system has occurred, the continued use of tryparsamide and bismuth is warranted. A patient with the meningovascular type of neurosyphilis eventually may show predominant signs of tabes dorsalis or dementia paralytica; hence the treatment planned must be directed toward the prevention of the development of these manifestations of neurosyphilis. If a course of tryparsamide and bismuth is planned, it will be necessary to give approximately 100 injections of each drug in order to arrest the disease. Fever therapy will accomplish the same result in less than half the time. Accordingly, if after a fair trial (three courses of tryparsamide and a bismuth compound) the clinical and serologic response has been unsatisfactory, fever therapy should be given. The bismuth compound and mapharsen may be given in alternating courses without a rest period, although the therapeutic efficiency is less from this combination than from tryparsamide and bismuth, intraspinal treatment or fever therapy. In other words, a patient with meningovascular neurosyphilis needs more intensive therapy than that offered by mapharsen and preparations of bismuth.

2. This patient may have become intolerant to arsenic. However, before accepting this as a fact it would be advisable to use some other arsenical preparation. Neoarsphenamine or arsphenamine should be tried, a small amount of the drug being given and a larger dilution (20 cc. to 0.1 gm.) used, and the injection should be given slowly. The bismuth injections should be continued. The fact that the blood tests have become negative is not, of course, sufficient reason to discontinue treatment.

There are some paradoxical phenomena in this case report. It is difficult, for instance, to understand why the condyloma lata would not melt away under the amount of treatment given, especially since the serologic reaction has reversed to negative so rapidly. The lesions may be condylomata acuminata, not of syphilitic origin. If the lesions are condylomata lata, they are still infectious, of course, and the negative serologic reports are in error. Rather than cauterize the lesions now it would seem advisable to continue with treatment for the syphilis and observe the effect on the lesions in order to determine their exact nature. This patient should have a spinal fluid examination at this time.

ASTHMA

To the Editor:—A man aged 46 has had asthma for about two years; for the last year it has completely disabled him from work. Two sisters had hay fever. Two years ago he was having the attacks both day and night; he had one or two every day, the worst spells coming after retiring between 10 p. m. and 6 a. m. Usually the attacks appeared two or three hours after he went to bed. Examination showed numerous bilateral nasal polyps with both antrums cloudy. These polyps were removed and antrum operations were done on both sides. Since then the nose has been open, no polyps have reformed and there has been no discharge from the nose. The rest of his physical examination, including a roentgenogram of the heart and an electrocardiogram, was negative. Intradermal skin tests showed him sensitive to house dust, all the fall pollens, cotton, cat hair, dog hair, goat hair, mule and horse dander, goose and duck feathers, kapok, all fish and a few foods. All the offending agents possible were removed from his environment and his diet was changed. He was given thirty injections of a stock dust extract, which apparently helped him. (He can stay in the house now while sweeping is being done.) Last fall I started on a polyvalent extract of about ten fall pollens. To date he has apparently had no trouble from the pollens, while last year from the tenth of August to about the middle of October he had asthma continuously. He has changed to a straw bed and straw pillows with rubber coverings for both and for a few nights has slept without any covers. He has returned to work regularly, but almost every night he has an attack of asthma between 11 and 2. A peculiar feature is that he worked for about ten nights and had his attacks just the same. He states that they were not so bad, but he attributes this to the fact that he took epinephrine as soon as he felt the attack coming on, while at home, asleep, he never takes it until he has to. For six months now he has had attacks only at night. In addition to the substances mentioned he had about 200 other tests, all of which were negative.

M. W. Haws, M.D., Fulton, Ky.

ANSWER.—Nocturnal asthma, with freedom during the day, is not uncommon. In fact, if asthma is mild it is usual to have attacks occur only at night. This does not necessarily indicate contact with an atopen in the bedroom. The cause for the greater susceptibility at night is not known. A number of explanations, as fatigue, postural effects, and changes in the autonomic nervous system (vagotonia), have been suggested as explanations. The occurrence of these attacks does indicate that the asthma has been only partially controlled. One may hazard an opinion that more intensive control of the atopic factors will probably lead to increased relief. While it may be difficult to do, it is neither impossible nor impracticable, if the illness warrants it, to remove completely all the offending environmental substances to which the patient reacts. Adequate measures should be taken to protect the patient from house dust especially. This substance originates primarily from deterioration of furniture stuffing and mattresses. The measures taken to cover the mattress and pillows are sufficient, if the covering does not leak through the seams. If upholstered furniture is present in the living room or bedroom, it must be replaced by cane or wooden furniture or furniture upholstered with horsehair. (Even patients sensitive to horse dander are not sensitive to horsehair after its preparation for use in furniture.) This furniture must contain neither cotton batting nor kapok. Both cotton and kapok are potent antigens and may easily be overlooked in such obscure places as stuffed toys, cotton filled comforters, automobile upholstery and even the padding of clothes. The use of cottonseed oil, as in fried potatoes, bakery goods or mayonnaise, must not be overlooked. Similar care must be exerted in the elimination of the other atopens to which this patient reacts. In addition to these measures and the continued treatment with pollen, one might add house dust hyposensitization, since, in spite of the removal of house dust from the patient's home, the contact with it in ordinary social life may be sufficient to cause him trouble. The usual measures for symptomatic relief should be continued.

PROBABLE LESION OF SACRAL ROOTS

To the Editor:—A man aged 28 complains of excruciating pain of five years' duration, beginning in the left half of the penis and radiating to the left testicle and left hip joint. At the time of the pain a noticeable depression as well as marked sweating in the left half of the penis approximately one-half inch from the corona was noticed. A month before the onset the patient's foot slipped while he was fixing a shower and he landed flat on his back. He was momentarily stunned. His neck struck the side of a curved end of a washtub. There was numbness in the left leg for a month. The patient has seen many doctors. Cystoscopic examinations were negative. There was no history of gonorrhea or syphilis; all smears were negative as well as blood tests. Roentgenograms of the hip were negative; roentgenograms of the bladder and kidneys were negative for stones. The patient describes the radiating pain to the left testicle as a knot between the rectum and the testicles. What diagnosis can you offer?

H. J. VALENTA, M.D., Tonopah, Nev.

ANSWER.—The results of a neurologic examination including a careful sensory examination would be helpful. The areas involved would coincide with the second, third and fourth sacral roots forming the cauda equina or the sacral and pudendal plexus. Because of the history of injury and subsequent numbness of the left leg, one should rule out the presence of an organic lesion causing compression or irritation of the roots involved. A careful x-ray examination of the sacral and lumbar spine should be made. A reverse Queckenstedt to rule out the presence of a blocking lesion should also be done. In the absence of any positive manifestation the most likely diagnosis would be a pudendal and testicular neuralgia, which is a rare condition and resistant to therapy.

Some of the procedures to be tried in therapy should be large doses of vitamin B, an epidural injection of from 10 to 20 cc. of 1 per cent procaine hydrochloride solution followed by from 50 to 100 cc. of physiologic solution of sodium chloride. If this is unsuccessful an injection of procaine hydrochloride into the sacral foramina of the involved roots may be tried. If this gives temporary relief, alcohol might be used in the same areas. In the absence of relief from any of these measures, surgical means might be necessary, such as cutting the involved posterior sacral roots or a chordotomy.

HYPOTONIC SOLUTIONS OF SODIUM CHLORIDE

To the Editor:—Can you give me any information concerning the result of treatment of encephalitis and other diseases as written up in a recent issue of *Collier's Magazine* and carried out by Dr. George M. Retan? One of my patients whose husband is suffering from the after-effects of this disease has asked me to give this treatment to him.

M.D., Massachusetts.

ANSWER.—Hypertonic solutions of sodium chloride have been used extensively in medicine for many different purposes and in the treatment of a variety of conditions. Hypotonic solution of sodium chloride, with which Retan reported such excellent results in acute anterior poliomyelitis, has not been used so extensively. An article in *THE JOURNAL*, June 1, 1935, advocated the use of such solutions in the treatment of some mental disorders such as dementia praecox.

There have been many studies in experimental physiology on the effects of hypotonic solutions, all of which suggest caution in their use even though much of the experimentation has been in vitro. The danger would seem to consist primarily in large amounts of hypotonic solutions which might lake the blood. No record of any confirmation of Retan's work has been obtained.

NO AUTOINTOXICATION FROM BREAST MILK

To the Editor:—1. Is there such a thing as autointoxication from breast milk in a nursing mother? 2. Could such a condition account for a high rise in temperature (105.4)? 3. What is the nature of the toxin produced, if any? 4. Should breast feedings be discontinued? Why? 5. What mode of therapy do you suggest?

M.D., New York.

ANSWER.—1. There is no such thing as autointoxication from breast milk in a nursing mother.

2 and 3. It was erroneously believed formerly that the establishment of milk secretion was accompanied by fever. The onset of puerperal fever on the third or fourth day, at about the time the congestion and enlargement of the breasts, at the beginning of lactation, takes place, gave rise to the belief that the congestion of the breasts caused the fever; hence the term "milk fever." There is, however, no inflammatory factor involved in this physiologic swelling of the breasts. No condition of lactation could account for a rise of temperature to 105.4 F. except an actual infection in the breast (mastitis) possibly leading to an abscess, or an infection elsewhere in the body. If occurring during the puerperium, puerperal fever or pyelitis must be seriously considered.

4. Breast feedings should be discontinued during a febrile period in the mother only if there is infection in the breast (mastitis) or if the mother's condition is critical or if she has some infectious disease.

5. The treatment of the fever depends on its cause. It is never due to autointoxication from breast milk.

SEROLOGICALLY LATENT SYPHILIS

To the Editor:—A white man aged 35 gives a history of having a chancroid infection in 1936. At that time the Kahn reaction of the blood was found to be positive and from September 1936 to February 1937 he received eighteen doses of nearsphenamine 0.06 Gm. and twelve doses each of bismuth subsalicylate and mercury. This treatment consisted of an arm injection and a hip injection each week, ending with six extra hip injections. Several blood tests were taken and all were reported negative. The patient was advised to have a spinal puncture and if this was negative he could consider himself cured. However, spinal puncture was not done. A recent newspaper article convinced the patient that perhaps he was not cured. I saw him for the first time two weeks ago. Other than for the foregoing facts, the history was essentially negative. Physical examination and the blood Kahn, globulin and gum mastic tests were negative; the spinal fluid showed a cell count of 3. I have classified this as a case of serologically latent syphilis and in view of its short duration have suggested continuous treatment as for early syphilis along the lines suggested in the manual of information for physicians on the treatment of syphilis published by the American Medical Association. At the time of the chancroidal infection dark field examination of the lesion was positive for the spirochete of syphilis. The patient is opposed to so much treatment but I have refused any treatment that falls short of that outlined. I would appreciate your criticism of my plan of treatment and would welcome any suggestions.

M.D., Tennessee.

ANSWER.—The so-called 'chancroid' in 1936 was obviously seropositive primary syphilis, in view of the fact that dark field examination at the time was positive and the blood serologic test was positive. The treatment given from September 1936 to February 1937 was inadequate both in amount and in kind. With only this amount of treatment there is still approximately a 50 per cent chance that the patient is not 'cured' and that subsequently, in spite of the fact that he is now clinically and serologically negative, he will ultimately have some form of progression or relapse. Under these circumstances he should receive one year of continuous treatment dating from this point, the treatment consisting of alternating courses of an arsphenamine and a bismuth compound by the system outlined by the Cooperative Clinical Group.

PREPARATIONS FOR TREATMENT OF MYCOTIC INFECTIONS

To the Editor:—Can you give me the uses of the following formulas in the *Pharmaceutical Recipe Book* (1936 edition)? Page 74: camphor 7.5, menthol 15, boric acid 15, sodium bicarbonate 15, alcohol 250, water a sufficient quantity to make 1,000 cc. Page 148: menthol in a fine powder 10, salicylic acid in a fine powder 10, petrolatum 980, to make 1,000. Menthol, camphor and eucalyptol ointment: menthol 8, camphor 8, eucalyptol 28, petrolatum 956, to make 1,000. Page 192: Conspergent powder with camphor and salicylic acid: camphor in a fine powder 30, salicylic acid in a fine powder 30, conspergent powder (R. B.) 940, to make 1,000. Is there any evidence in the past literature that these preparations have been used successfully or have clinically revealed some unusual success in the treatment of the mycotic disorders either of the hairy or of the glabrous skin, especially when either one of the preparations was used alone and not as adjuvant therapy with other forms of treatment?

DOUGLAS T. PRENN, M.D., New York.

ANSWER.—The *Pharmaceutical Recipe Book* is edited by a committee of the American Pharmaceutical Association and contains only formulas that have been thoroughly tried somewhere in the United States and have been proved effective. The one on page 74 of the 1936 edition is an evaporating lotion made more cooling and analgesic by the camphor and menthol. It would have little effect on the growth of fungi but might be used to counteract the itching and burning sensations and to reduce inflammation in fungous infections. The first formula on page 148, 1 per cent each of menthol and salicylic acid in petrolatum, might be used as a mild fungicidal. The second one on this page, 0.8 per cent of camphor and menthol and 2.8 per cent of eucalyptol in petrolatum, would have the same action. Probably the activity would vary with different organisms.

"Conspergent" is a word not in Webster's unabridged dictionary or in any other consulted but is evidently related to "conspere," a term used in entomology to designate "many spotted," derived from a word meaning "sprinkled." The conspergent powder mentioned is composed of 150 parts of boric acid, 350 parts of zinc oxide and 500 parts of purified talc. In short, it is a dusting powder. Camphor and salicylic

acid, each 3 per cent, in this would make a good preparation for use in cases of ringworm, particularly for use in moist situations, as between the toes. It would be mildly fungistatic.

All these preparations might be useful in the treatment of fungous infections of the surface of the glabrous skin and in tender hairy parts, as the axillas and pubic regions.

REDUCTION IN VISUAL FIELD FOR GREEN NOT SIGN OF FOCAL INFECTION

To the Editor:—During the last annual meeting of the Indiana State Dental Association Dr. Louis Hill of Los Angeles made the following statements: 1. In the presence of foci of infection anywhere in the body there is produced a reduction in the green field in the perimetry test. 2. The dentist should refer the patient to a competent optometrist for a perimetry test and if the optometrist found a diminution of the green field it meant "foci of infection." Then the optometrist should refer the patient back to the dentist for a thorough dental examination to see whether the focus is of dental origin. If the dentist could not find any dental focus he should refer the patient to a physician, who in turn would try to locate the focus. Dr. Hill pointed out that in this manner dentists, physicians and optometrists could work harmoniously in solving the problems of foci of infection. Dr. Hill also commented on a case in which the physician refused to be a party to such a scientific investigation, illustrating the lack of cooperation on the physician's part. I have investigated this idea, consulting some of the leading ophthalmologists at Indiana University School of Medicine, and they state that they are totally ignorant of the value of such a test for foci of infection. What is your opinion on the value of such a test?

JOHN W. GRAVES, M.D., Indianapolis.

ANSWER:—It is certainly not true that a reduction in the visual field for green indicates a focus of infection. Defects in the visual field result, of course, from a number of causes, and absorption from a focus of infection is not one of the more common of these. A record of the fields for color is a procedure depending in part on the subjective judgment of the patient and it is common to find the field for green reduced during the first examination of a normal person who later shows normal fields. If a patient should be referred to a physician with no other finding than a reduction in the green field as measured by an optometrist, he would be justified in trusting his own clinical judgment as to the necessity of a thorough search for foci of infection. It would be entirely misleading if a dentist, suspecting focal infection, should depend on perimetric examination to decide the matter.

PARALYSIS NOT RELATED TO THYROIDECTOMY

To the Editor:—A woman aged 56 had a thyroidectomy in 1936. About two weeks afterward the following symptoms appeared: difficulty in swallowing, loss of voice, saliva running from the mouth, drooping of the lower lip—a glossopharyngeal paralysis gradually growing worse. Could there be any connection between the loss of the thyroid and the subsequent paralysis?

M.D., California.

ANSWER:—It is obvious that no paralysis such as that described as having occurred in this patient could have been the result of an error described in surgical technique. One cannot be certain from the symptoms that the patient suffered from glossopharyngeal paralysis, as this is a rare condition and difficult to diagnose. In a woman of 56 it seems much more likely that there is a bulbar palsy or bulbar neuritis. The fact that it occurred two weeks afterward would speak for thrombosis of some small vessel in the pons. One should consider the remote possibility of metastasis from a malignant thyroid, although such metastases are extremely rare in the brain.

ENDOTHELIOMA OF PLEURA

To the Editor:—I should appreciate information on endothelioma of the pleural cavity.

M.D., Ohio.

ANSWER:—Endothelioma of the pleura is a malignant tumor originating from the endothelial covering of the pleura. It may be limited to the costal pleura. It forms tumorous masses over the pleural cavity, which may be recognized radiologically after pneumothorax has been done. The main clinical feature is the development of an exudate, which is in most instances hemorrhagic. The presence of a hemorrhagic exudate is always suggestive of either neoplastic metastasis to the pleura or primary endothelioma of the pleura. The clinical symptoms are those of a pleurisy, particularly in the early stages, with pain which improves with the formation of an exudate and reappears after tapping. The exudate usually reappears rapidly after thoracentesis. The treatment is mainly limited to palliative procedures. Irradiation sometimes retards the reappearance of the exudate but as yet has not produced a cure.

TEMPERATURE RECORDING WITH A STANDARD THERMOMETER

To the Editor:—In taking temperature with the ordinary thermometer, which is usually standardized for one minute, one reading is obtained when it is left in the mouth for one minute and another reading, usually half a degree higher, on waiting three minutes. It has always been my impression that these thermometers are standardized to one minute and that the correct way to take the temperature is to leave it in the patient's mouth one minute. If it is left in for three minutes, a considerable discrepancy occurs. Which method should be used to obtain the correct body temperature?

M.D., California.

ANSWER:—To get the true temperature reading a clinical thermometer should be left in the patient's mouth at least three minutes; five minutes would be better. This is the opinion of the Bureau of Standards.

A general statement cannot be made as to the length of time necessary for any clinical thermometer to give a true temperature reading. The time varies with the thermometer used and with the conditions of the patient's mouth at the time. Obviously, in some cases one minute might be enough. However, the only way to be sure is to try a longer time. If the reading of the thermometer goes up on the second trial, it is apparent that the time of the first trial was not long enough. The length of time should be increased until the reading does not change with the increase of time.

PROSTATIC CONGESTION AND ORGASM

To the Editor:—A man aged 34, married and the father of four children, has a negative venereal history and is in excellent general health except for a spastic descending colon. He has a disturbance of the orgasm. At 17 in an effort to break the habit of masturbation he held back the ejaculation (masturbatio incompleta). He states that at these times the ejaculate consisted of a small amount of jelly-like material. Shortly afterward came his first intercourse, when he says he was left wondering whether he had completed the act. In this case and in all intercourse since, the ejaculate has consisted of a small amount of thick colorless material and the sensation has been that of an uncompleted act. He says that the ejaculation is not premature as to time consumed and that at the onset of intercourse, in which he indulges once or twice a week, the organ is rigid and normal and remains so until the act is completed, when it gradually becomes flaccid. The chief unusual feature of this case is that nocturnal emissions are normal and that it is at this time only that the orgasm is complete. Prostatic massage shows a gland normal in size and not unduly tender; the secretion shows 4 plus leukocytes and numerous clumps of pus cells. This condition has not improved with massage over a long period. Urethroscope examination shows a normal posterior urethra. I have tried massage and silver instillations (Hühner), sedatives, stimulants and various gland preparations but all to no avail. As I see it, the ejaculation in this case consists of the emptying of the seminal vesicles alone without the prostate and other glands performing their parts of the act. Is such a condition possible and if so how can it be corrected?

M.D., Minnesota.

ANSWER:—If the examination of the prostatic urethra performed without the use of any local anesthetic showed a normal prostatic urethra without any congestion present, the case must be considered psychic in character and should be treated by a specialist in psychiatric conditions. Many urologists, however, employ as a routine a local anesthetic which has the effect of blanching the mucous membranes and may thus cause a congestion to be missed.

ACAROPHOBIA

To the Editor:—The enclosed samples are from the skin of a patient. I cannot vouch for the authenticity of these, as she brought them to the office; however, she has expressed small ones of similar appearance in my presence. For the last year she has had typical menopausal symptoms. These are under control with theelin; liver therapy has corrected the anemia. Her only physical abnormalities now are a moderate prolapse of the uterus, irregular menses and an occasional staphylococcal infection of the skin, scarcely enough to be called furunculosis. Repeated Wassermann tests have been negative; all laboratory tests for blood and urine are now normal. Symptomatically she says there is a crawling sensation in her skin and then these little black objects hop out. She says she also passes them vaginally and rectally. There is no evident skin lesion prior to the appearance of one of these objects on the surface. Crushed under a cover glass they appear to look like an amorphous sulfide. Is there a name for this condition or a cause? Any information will be appreciated.

M.D., Alabama.

ANSWER:—This patient has acarophobia, a psychic disorder in which the patient erroneously believes and maintains that the skin is contaminated by some parasite. This eruption is a part of the general group of cutaneous neuroses, a group of eruptions which have a variety of expressions of an abnormal psyche on the skin. These patients frequently present hyperesthesia in association with hysteria. Mental disorders and depressing mental influences play a certain part in the causation of this condition.

Medical Examinations and Licensure

COMING EXAMINATIONS

STATE AND TERRITORIAL BOARDS

ALABAMA: Montgomery, Jan. 3-5 and June 20-22. Sec., Dr. J. N. Baker, 517 Dexter Ave., Montgomery.

ALASKA: Juneau, March 2. Sec., Dr. W. W. Council, Box 561, Juneau.

ARIZONA: *Basic Science*. Tucson, Dec. 20. Sec., Dr. Robert L. Nugent, Science Hall, University of Arizona, Tucson.

CALIFORNIA: *Reciprocity*. Los Angeles, Nov. 16. Sec., Dr. Charles B. Pinkham, 420 State Office Bldg., Sacramento.

COLORADO: *Basic Science*. Denver, Dec. 7-8. Sec., Dr. Esther B. Starks, 1459 Ogden St., Denver.

DELAWARE: Dover, July 11-13. Sec., Medical Council of Delaware, Dr. Joseph S. McDaniel, 229 S. State St., Dover.

DISTRICT OF COLUMBIA: *Basic Science*. Washington, Dec. 26-27. *Medical*. Washington, Jan. 9-10. Sec., Commission on Licensure, Dr. George C. Ruhland, 203 District Bldg., Washington.

FLORIDA: Jacksonville, Nov. 14-15. Sec., Dr. William M. Rowlett, Box 786, Tampa.

INDIANA: Indianapolis, June 20-22. Sec., Board of Medical Registration and Examination, Dr. J. W. Bowers, 301 State House, Indianapolis.

KANSAS: Topeka, Dec. 13-14. Sec., Board of Medical Registration and Examination, Dr. J. F. Hassig, 905 North 7th St., Kansas City.

KENTUCKY: Louisville, Dec. 6-8. Sec., State Board of Health, Dr. A. T. McCormack, 620 S. Third St., Louisville.

MARYLAND: *Medical (Regular)*. Baltimore, Dec. 13-16. Sec., Dr. John T. O'Mara, 1215 Cathedral St., Baltimore. *Medical (Hæmopathic)*. Baltimore, Dec. 13-14. Sec., Dr. John A. Evans, 612 W. 40th St., Baltimore.

MISSISSIPPI: *Reciprocity*. Jackson, December. Asst. Sec., State Board of Health, Dr. R. N. Whitfield, Jackson.

NEBRASKA: Lincoln, Nov. 25-26. Dir., Bureau of Examining Boards, Mrs. Clark Perkins, State House, Lincoln.

NEW HAMPSHIRE: Concord, March 9-10. Sec., Board of Registration in Medicine, Dr. Fred E. Clow, State House, Concord.

NEW YORK: Albany, Buffalo, New York and Syracuse, Jan. 23-26. Chief, Bureau of Professional Examinations, Mr. Herbert J. Hamilton, 315 Education Bldg., Albany.

NORTH CAROLINA: *Reciprocity*. Raleigh, December. *Examination*. Raleigh, June 19. Sec., Dr. William D. James, The Hamlet Hospital, Hamlet.

NORTH DAKOTA: Grand Forks, Jan. 3-6. Sec., Dr. G. M. Williamson, 4½ S. Third St., Grand Forks.

OHIO: Columbus, Dec. 7-9. Sec., State Medical Board, Dr. H. M. Platter, 21 W. Broad St., Columbus.

OKLAHOMA: *Basic Science*. Oklahoma City, Nov. 30. Sec. of State, Hon. Frank C. Carter, State Capitol Bldg., Oklahoma City. *Medical*. Oklahoma City, Dec. 14. Sec., Dr. James D. Osborn Jr., Frederick.

OREGON: *Basic Science*. Portland, Nov. 19. Sec., State Board of Higher Education, Mr. Charles D. Byrne, University of Oregon, Eugene.

PENNSYLVANIA: Philadelphia, January. Sec., Board of Medical Education and Licensure, Dr. James A. Newpher, 400 Education Bldg., Harrisburg.

PUERTO RICO: San Juan, March 7. Sec., Dr. O. Costa Mandry, Department of Health, San Juan.

SOUTH DAKOTA: Pierre, Jan. 17-18. Director of Medical Licensure, Dr. B. A. Dyar, State Board of Health, Pierre.

TEXAS: Houston, Nov. 14-16. Sec., Dr. T. J. Crowe, 918-20 Mercantile Bldg., Dallas.

VERMONT: Burlington, Feb. 14. Sec., Board of Medical Registration, Dr. W. Scott Nay, Underhill.

VIRGINIA: Richmond, Dec. 14-16. Sec., Dr. J. W. Preston, 30½ Franklin Road, Roanoke.

WISCONSIN: *Basic Science*. Milwaukee, Dec. 3. Sec., Prof. Robert N. Bauer, 3414 W. Wisconsin Ave., Milwaukee. *Medical*. Madison, Jan. 10-14. Sec., Dr. Henry J. Gramling, 2203 S. Layton Blvd., Milwaukee.

NATIONAL BOARD OF MEDICAL EXAMINERS SPECIAL BOARDS

Examinations of the National Board of Medical Examiners and Special Boards were published in THE JOURNAL, November 5, page 1789.

Tennessee June Examination

Dr. H. W. Qualls, secretary, Tennessee State Board of Medical Examiners, reports the written examination held at Knoxville, Memphis and Nashville, June 15-16, 1938. The examination covered ten subjects and included 100 questions. An average of 75 per cent was required to pass. One hundred and three candidates were examined, 100 of whom passed and three failed. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
Howard University College of Medicine....(1937)	84.3, 84.9, 85.8, 87.3		
Emory University School of Medicine.....(1938)	85.8		
Tulane University of Louisiana School of Medicine....(1938)	83.3, 84.2		
St. Louis University School of Medicine.....(1938)	84.7, 85.4, 86.3, 86.4, 86.6, 87.3, 87.7, 87.8, 87.9, 88.2		
University of Pennsylvania School of Medicine.....(1937)	87.3		
Meharry Medical College.....(1935)	84.1, (1938) 80.6, 82.3, 82.8, 83.2, 83.8, 84.2, 84.4, 84.6, 85.1, 85.2, 85.4, 85.5, 85.5, 85.5, 85.7, 85.7, 85.7, 85.8, 86, 86.2, 86.4, 86.6, 86.9, 87.3, 87.4, 87.6, 88, 88.7, 89.1, 89.2, 89.6		
University of Tennessee College of Medicine.....(1938)	83.5, 84.7, 85.2, 85.5, 85.8, 86.4, 86.5, 87.2, 87.5		

Vanderbilt University School of Medicine.....(1938)	84.6, 84.7, 84.8, 85, 85.3, 85.3, 85.9, 86.1, 86.5, 86.5, 86.6, 86.7, 86.8, 87, 87.1, 87.1, 87.2, 87.2, 87.3, 87.3, 87.3, 87.5, 87.6, 87.6, 87.6, 87.7, 87.8, 87.9, 88, 88.1, 88.1, 88.3, 88.4, 88.6, 88.7, 88.8, 88.8, 89.8		
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School	FAILED	Year Grad.
Meharry Medical College	(1938, 2)	
Regia Università di Napoli Facoltà di Medicina e Chirurgia.....	(1936)	

Eight physicians were licensed by endorsement from June 2 through August 29. The following schools were represented:

School	LICENSED BY ENDORSEMENT	Year Endorsement Grad. of
University of Georgia School of Medicine.....(1936)	Georgia	
Rush Medical College	(1930) W. Virginia	
University of Illinois College of Medicine.....(1931)	Missouri	
Tulane University of Louisiana School of Medicine....(1928)	Louisiana	
Johns Hopkins University School of Medicine.....(1934)	Maryland	
University of Minnesota Medical School.....(1935)	N. B. M. Ex.	
University of Cincinnati College of Medicine.....(1935)	Ohio	
Licentiate of the Royal College of Physicians, of the Royal College of Surgeons, Edinburgh, and of the Royal Faculty of Physicians and Surgeons, Glasgow (1928)	N. B. M. Ex.	

Delaware July Report

Dr. Joseph S. McDaniel, secretary, Medical Council of Delaware, reports the written examination held at Dover, July 12-14, 1938. The examination covered ten subjects and included 100 questions. A grade of 75 per cent in each subject was required to pass. Fourteen candidates were examined, all of whom passed. Five physicians were licensed by reciprocity July 19. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
Georgetown University School of Medicine.....(1937)	77.8		
Johns Hopkins University School of Medicine.....(1931)	80.9, (1932) 78, (1936) 82.6		
University of Nebraska College of Medicine.....(1937)	80.6		
Columbia University College of Physicians and Surgeons	(1936) 80.3		
Hahnemann Medical College and Hospital of Philadelphia	84.6, 84.6		
Jefferson Medical ..	80.6		
Temple University ..	82.3		
University of Pennsylvania School of Medicine.....(1936)	80.3		
University of Virginia Department of Medicine.....(1937)	84.9		

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
Howard University College of Medicine.....(1926)	W. Virginia		
Hahnemann Medical College and Hospital of Philadelphia	(1899) Penna.		
Jefferson Medical College of Philadelphia.....(1926)	Penna.		
Meharry Medical College.....(1934)	Tennessee		
Trinity Medical College, Toronto.....(1895)	Penna.		

Oklahoma June Examination

Dr. James D. Osborn Jr., secretary, Oklahoma State Board of Medical Examiners, reports the written examination held at Oklahoma City, June 8-9, 1938. The examination covered twelve subjects and included 120 questions. An average of 75 per cent was required to pass. Forty-six candidates were examined, all of whom passed. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
Creighton University School of Medicine.....(1938)	84*		
University of Oklahoma School of Medicine.....(1934)	84, (1937) 80, (1938) 77*, 78*, 78.9*, 79*, 80*, 80*, 80*, 81*, 81*, 81*, 81.9*, 82*, 82*, 82*, 82*, 82.8*, 82.9*, 82.9*, 83*, 83*, 83*, 83*, 83*, 83*, 83*, 83*, 83*, 83*, 83*, 83*, 84*, 84*, 84*, 84*, 85*, 85*, 85*, 85*, 85*, 85*, 85.8*, 86*		

Sixteen physicians were licensed by reciprocity from June 13 through August 3. The following schools were represented:

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
University of Arkansas School of Medicine.....(1930)	W. Virginia		
State University of Iowa College of Medicine.....(1934)	Iowa		
University of Kansas School of Medicine.....(1934), (1935)	Kansas		
Tulane University of Louisiana School of Medicine.....(1926)	Mississippi		
Johns Hopkins University School of Medicine.....(1920)	Virginia		
Washington University School of Medicine.....(1927), (1934), (1936) Missouri	Ohio		
Hahnemann Medical College and Hospital of Philadelphia.....(1937)	Tennessee		
Vanderbilt University School of Medicine.....(1937)	Texas		
University of Texas School of Medicine.....(1929), (1931)	Virginia		
Medical College of Virginia.....(1931)	Virginia		
University of Virginia Department of Medicine.....(1933)	Wisconsin		
University of Wisconsin Medical School.....(1932)	Wisconsin		

* License withheld pending completion of internship.

Book Notices

The Prevention of Puerperal Sepsis. By L. Colebrook, M.B. B.S., Hon. Director Research Laboratories, Queen Charlotte's Hospital, London. Antisepsis in Midwifery. By L. Colebrook and W. R. Maxted. With a foreword by Sir Comyns Berkeley, M.C., M.D., F.R.C.P. Reprinted from the *Journal of Obstetrics and Gynaecology of the British Empire*, Vol. XLIII, 1936, pp. 691-714. Paper. Price, \$1. Pp. 109. New York, Toronto & London: Oxford University Press, 1938.

This booklet consists of reprints of the two articles whose titles appear in the caption. These articles were published in the *Journal of Obstetrics and Gynaecology of the British Empire* in 1933 and 1936. The authors express opinions which have been recognized and accepted by many observers since the time of Gordon, Semmelweis and Holmes. That puerperal sepsis is essentially a contact infection has been almost universally accepted. While some have stressed the possibility of so-called autogenous infection, most authorities have continued to believe that such infection is the exception and not the rule. That some variety of streptococcus is responsible for most of the fatal cases of puerperal infection has been known since the time of Pasteur. The authors have added further proof of the correctness of certain principles which have been established and practiced by many clinicians and in well conducted maternity hospitals. One great difficulty has been and still is that well known principles of prevention of this contact and wound infection have not been generally applied. The authors properly call attention to the many lapses in good surgical technic in obstetric practice. The proper use of asepsis in the preparation of the patient, the material and the personnel is essential, and its omission is serious negligence. The proper use of masks and gloves is part and parcel of good technic. The exclusion of carriers is vital for the welfare of both mother and baby. It is difficult for one grounded in the theory of asepsis to revert to the idea of reliance on chemical antisepsis. One should be open minded and cherish the hope that some chemical antiseptic will eventually be found which will maintain an aseptic field without interfering with the immune reactions of the tissues.

The authors seem to feel that iodine and the preparation of a xylenol derivative are efficacious in combating infection, especially that with hemolytic streptococci. One should hesitate to rely on either of these agents to the exclusion of other well established methods of securing and maintaining an aseptic field. The authors would doubtless be the first to sustain the argument for thorough obstetric technic and yet the summary of conclusions seems to be offering makeshift methods in obstetric practice. The suggestions that thorough washing of the hands, which cannot be done in three or five minutes, be omitted, that rubber gloves, water and utensils be sterilized by means other than boiling, savors of the makeshift. The surgical technic employed during labor and delivery should be the equivalent of that used in opening the abdomen.

The principles enunciated throughout the text are excellent and no one can fail to profit by careful study and the application of the procedures advocated. The authors are to be complimented on their contribution to this important aspect of preventive medicine.

Le traitement de la tuberculose pulmonaire par la tuberculine. Par le Dr. M. Jaquerod. Paper. Pp. 43, with 2 illustrations. Lausanne: Librairie Payot & Cie. 1937.

This paper covered monograph in French summarizes Jaquerod's experiences and views on tuberculin therapy in general and particularly in pulmonary tuberculosis. His experiences date back as far as 1903 and were reported variously in 1905, 1909, 1912 and 1920 in the *Revue médicale de la Suisse Romande*. In the introduction he notes that viable bacilli and tuberculins (old tuberculin and bacillus emulsion) differ in action and briefly reviews the tuberculin treatment of pulmonary tuberculosis. The nature of tuberculin (old tuberculin and bacillus emulsion) and its toxic action is detailed, as well as the therapeutic action based on the conception of a toxic tuberculin reaction (the focal reaction) and an antituberculin immunization. Contraindications in certain types of tuberculosis, such as the danger of focal reactions in intestinal tuberculosis, are pointed out. In well chosen clinical cases, tuberculin treatment has a place, he believes. He employs it, beginning

with very small but gradually increasing doses of old tuberculin and transferring to equivalent bacillus emulsion, when indicated, according to his scheme of therapy. The scheme of treatment is outlined generally and the cutaneous reactions are evaluated. All in all, whether or not one agrees with the theoretical basis of this treatment, one must admit that this report of thirty-five years' experience in treating selected cases of pulmonary tuberculosis, successfully in some instances as presented by a few selected cases, makes the monograph worth reading, if one is conversant with French. The presentation is to be commended for its sincerity and patient evaluation. The author is well known in the field of tuberculosis for similar monographs on allied subjects in this field.

Hibernation and Marmot Physiology. By Francis G. Benedict, Director, Nutrition Laboratory, Carnegie Institution of Washington, and Robert C. Lee. Carnegie Institution of Washington Publication No. 497. Paper. Pp. 239, with 11 illustrations. Washington, D. C.: Carnegie Institution of Washington, 1938.

A number of important conclusions are drawn from work reported in this volume: (1) that the respiratory quotient of the marmot gives no evidence of carbohydrate synthesis from fat; (2) that the metabolism in hibernation is qualitatively the same as in the fasting state; (3) that the metabolism is greater in hibernation than in cold-blooded animals of the same size; (4) that although carbon dioxide narcosis produces a state similar to hibernation, the authors believe the two are not identical; (5) that much work needs to be done to clarify the mechanism of hibernation. The merit in the work is mainly in repeating under conditions of careful control what had been done by other experimenters. The discussion is wordy and sometimes uncritical. For example they say "From our long experience in studying the effect of muscular activity of itself upon metabolism it is inconceivable to think that any appreciable percentage of the great increase in metabolism noted with the falling environmental temperature can be attributed to the relatively small increases noted in muscular activity. We are forced, therefore, to the conviction that in this case there is a true chemical regulation of heat production, i. e., an increase in heat production to combat the lower environmental temperature." This is in spite of the fact that no observations except by inspection were made of muscular movement. It is equally inconceivable that any one could determine by inspection whether shivering was or was not occurring to an extent sufficient to increase the metabolic rate. The authors' conclusion on this score seems highly debatable. The observations are carefully and completely recorded and the work is therefore of lasting value.

Nouvelle pratique dermatologique. Publiée par MM. Darier, Sabouraud, Gougerot, Millan, Pautrier, Ravaut, Sézary, Clément Simon. Secrétaire général, Clément Simon. Tome VI: Dermatose par carence. Atrophies et dystrophies. Tumeurs et naevi. Par P. Blum et al. Boards. Price, 300 francs. Pp. 954, with 269 illustrations. Paris: Masson & Cie, 1936.

The first forty pages in volume VI are devoted to the deficiency diseases. Nicolas and Massia under this heading group pellagra, the pellagroid erythemas and the pseudo-pellagras as the pellagra syndrome. This is followed by an article on beriberi and another on scurvy and on Barlow's disease (avitaminosis C).

Petges and his collaborators devote 197 pages to the cutaneous atrophies. Under the heading of vergetures are included all the various striae. Dermatite chronique atrophiante (Pick-Herxheimer) and anétoderma are discussed at length. The black and white and colored plates of the former could not be improved on. Poikiloderma has been the subject of so much discussion that any one especially interested in this disease would do well to read the exhaustive and authoritative treatment of this dermatosis by Gabriel and André Petges. This chapter is well documented and well illustrated. Particularly interesting are the roentgenograms of poikilodermatomyositis with calcareous concretions. The discussion of the differential diagnosis is a valuable contribution to the literature.

The melanosis of Riehl is treated at length by Petges and Lecoulant. In conclusion of the discussion on the pathogenesis they say "no pathogenesis is at present acceptable, one can make only hypotheses." The same authors also discuss the cicatricial atrophies of the skin. White spot disease is discussed by G. and A. Petges, and G. Petges and Lecoulant take up the senile atrophies and the colloid atrophies and the dystrophies. They

continue with the subjects of cutis laxa, elastic skin, pseudo-xanthoma elasticum of Darier and epidermolysis bullosa.

Paul Blum follows with an excellent chapter on the keratoses. Particularly valuable is the differentiation of ichthyosis and érythrodermie congénitale ichthyosiforme.

Périn follows with an article on Darier's disease. The excellent clinical illustrations and photomicrographs together with the discussion and the bibliography leave nothing to be desired. The same author does just as well by parakeratosis of Mibelli.

In a short article with reproductions of three excellent photographs Gougerot and Carraud give an excellent description of acanthosis nigricans and a differential diagnosis of that disease with the confluent papular papillomatosis, which they were the first to describe in 1928.

Primary cutaneous amyloidosis is beautifully presented with excellent illustrations by Nanta.

A noteworthy chapter of this volume is that of Périn on nevi, with an introduction by Darier. An interesting feature of this chapter is the inclusion of von Recklinghausen's disease in the nevus group. The hemangiomas and the lymphangiomas are included. The illustrations in color and in black and white are perfect.

A short article, well illustrated, on the benign epithelial tumors is contributed by Mlle. Dobkévitch. This is followed by an article on the cysts by Mlle. Eliaschew.

Woringer includes in his contribution the benign connective tissue tumors, myxomas, histiocytomas, lipomas, vaselinomas, paraffinomas, calcareous concretions, leiomyomas and dermatomyoma.

The remainder of the volume, 343 pages, is devoted to the precancerous dermatoses, epithelial tumors, sarcomas and the melanomas. Civatte opens the discussion with an exhaustive and beautifully illustrated presentation of the precancerous dermatoses. In the eighty-one pages allotted to him he takes up the subject of the etiology and physiopathology of these disorders. He continues with a scholarly dissertation on senile keratoses, xeroderma pigmentosum, Bowen's disease, erythroplasia, Paget's disease, érythro-kératodermies neviques pré-cancéreuses and epidermodysplasie verruciforme. The subjects are presented from the histopathologic side with the expertness that we have come to expect from Civatte. Although the histopathologic illustrations are mostly drawings, nothing is lost and much is gained thereby.

Following the work of Civatte come ninety-three pages devoted to the malignant epithelial tumors by Favre, Jossier and Martin. All phases of the subject are taken up in detail. The clinical and histopathologic illustrations in color and in black and white are beyond criticism. Favre and Jossier continue with a masterly presentation of the cutaneous sarcomas and their treatment. The authors do not include Kaposi's disease in the sarcoma group but discuss it as a sarcomatosis or as an angiomatosis both with question marks. Woringer presents the melanomas and Lacassagne closes with a discussion of all phases of the treatment of cancer of the skin.

In this volume the same high standard of excellence as characterized the preceding volumes has been maintained.

Practical Otolaryngology, Rhinology and Laryngology. By Adam Edward Schlanser, M.D., Colonel, Medical Corps, United States Army. Cloth. Price, \$4.50. Pp. 315, with 81 illustrations. Philadelphia: Lea & Febiger, 1938.

This little book, intended primarily for the army medical officer, is considered by the author also to have an appeal for the civilian practitioner because it is based on a peace time practice. Naturally when a book lays emphasis on its brevity and practicability it is to be expected that it will in large measure reflect the personal experiences of the author and this book is no exception. The danger, however, in this connection is that the author's likes and dislikes or his special predilections will receive undue emphasis. Most of the material presented in the book is accurate, concise and devoid of wearying technicalities, the approach being always from the clinical side. However, one cannot help but notice that whereas on the one hand a number of pages are given over to nasal deformities, a special topic requiring much more space than the author could afford to devote to it, on the other hand no mention is made of such important subjects as throat manifestations in connection with the various blood dyscrasias, the subject of sepsis due to

ear, nose or throat infections, the subject of osteomyelitis and the role of physical therapy in otolaryngology. Nevertheless, despite these inconsistencies, the book will find favor particularly with army officers, to whom the author is well known for his long and admirable service in various important capacities.

Medizinische Praxis: Sammlung für ärztliche Fortbildung. Herausgegeben von Prof. Dr. L. R. Grote, Leitender Arzt der Medizinischen Klinik des Rudolf-Hess-Krankenhauses Dresden. Prof. Dr. A. Fromme, Direktor der Chirurgischen Abteilung des Stadtkrankenhauses Dresden-Friedrichstadt, und Prof. Dr. K. Warnekros, Direktor der Staatlichen Frauenklinik zu Dresden. Band XIV: Elektrokardiographie für die ärztliche Praxis. 15 Vorlesungen zur Einführung in die elektrische Untersuchungsmethode des Herzens und ihre praktischen Ergebnisse bei rhythmischem und arrhythmischem Herzschlag. Von Prof. Dr. Erleli Boden. Fourth edition. Paper. Price, 10 marks. Pp. 192, with 104 illustrations. Dresden & Leipzig: Theodor Steinkopff, 1939.

This little monograph, which has gone through four editions in six years, is intended for the general practitioner. There have been only a few changes from the third edition and these have concerned themselves chiefly with the section dealing with intraventricular block, which has been recast. The author has taken cognizance of the recent controversy regarding the terminology of bundle branch block, which was precipitated in America, and properly concludes that the evidence for the nomenclature of right and left bundle branch block is not convincing and of but little practical importance. He consequently has made use of the term unilateral bundle branch block of the common and uncommon varieties. He has also substituted for so-called arborization block the term bilateral bundle branch block. As in the past editions, the most instructive part of the monograph is its clear diagrams, which introduce the reader to the fundamental concepts in electrocardiography. Only two substitutions of electrocardiographic plates have been made, and the criticism directed at previous editions that the electrocardiograms are not always the most suitable still applies. It is unfortunate that the author has not altered the section on coronary artery occlusion and has ignored the use of chest leads in diagnosing this condition. Not enough stress is laid on the importance of the electrocardiogram in this disease. This section as a result is very unsatisfactory. This monograph can therefore not be as suitable as some of the others recently published.

Adventures in Respiration: Modes of Asphyxiation and Methods of Resuscitation. By Yandell Henderson. Cloth. Price, \$3. Pp. 316, with 16 illustrations. Baltimore: Williams & Wilkins Company, 1938.

Whenever the word "adventures" appears in a title, the prospective reader fully relies on the author to produce engaging material. This book fulfils its title. It is replete with physiologic history, reminiscence and pertness combined with authoritative presentation of scientific investigations on respiration, asphyxiation and resuscitation. This is a book with flavor—Hendersonian flavor. Two synthetic quotations reflect the historical and reminiscent aspects of the book:

On the morning of May 9, 1794, in the Palace de la Revolution in Paris, Antoine Laurent Lavoisier died under the guillotine. The Republic, it was said, had no need of scientists. As the sharp stroke of the guillotine severed his neck, there passed away from this world in his fifty-first year this master mind of science, who had done so much to draw aside from truth the veil of man's ignorance and wrong thought.

In the second half of the nineteenth century, every young American physiologist aspired to round out his education by a year in Germany. There he experienced the masterly neglect of the German professors and learned that to pluck the fruit of learning from the highest branches one must climb the tree all by oneself, even if it is a tree that no one has ever climbed before. At home I met my "tree" immediately.

This book is a portrait of that tree. Combined with this sprightliness are many helpful facts, in twenty-seven chapters, on such topics as the fallacy of asphyxial acidosis, carbon monoxide asphyxia, mountain sickness and acclimatization, resuscitation of the newborn, the functional factor in pneumonia and failure of the circulation.

Characteristic of this able author, the book is pleasantly dogmatic. For instance, in the presence of recent publications alleging chronic carbon monoxide poisoning the author states that "there is no such condition as the expression chronic carbon monoxide poisoning would imply." Then with propriety he states that prolonged asphyxiation may lead to damage to the brain too deep for complete restoration, leading to survival, with impaired minds, loss of memory, paralyzes or sensory defects. He states that claims of impaired health from exposure

to carbon monoxide should not be accepted as valid unless there is (1) at least 50 per cent saturation of the blood, (2) exposure of from three to ten or more hours and (3) continuous, complete unconsciousness, lasting for six to twenty-four hours after return to fresh air. While others may be disposed to recite experiences to the contrary, this author's assurance carries conviction.

This book may be read with profit by all persons from the high school student to the medical college professor of physiology.

Subacute and Chronic Pericardial and Myocardial Lesions Due to Non-Penetrating Traumatic Injuries: A Clinical Study. By Erik Warburg, M.D., Professor of Internal Medicine in the University of Copenhagen. With a short biography of Oluf Borch (Olaus Borrichius). By Torben Geill, M.D., Physician-in-Chief, de Gamles By, Copenhagen. Translated by Dr. Hans Andersen and Dr. Gerda Seidelin. Cloth. Price, 12s. 6d.; 14 kroner. Pp. 147, with 19 illustrations. London: Oxford University Press: Copenhagen: Levin & Munksgaard, 1938.

This monograph is an exhaustive study of traumatic myocardial disease. As the author states in the introduction, when the physician is faced with the problem of a patient that may have developed cardiac disease following a blow on the chest or other trauma it is difficult to find detailed knowledge of this subject in an ordinary textbook. For this reason a book of this type fills a long felt want. The first chapter consists of some remarks on the history and the delimitation of the subject. The historical aspect is particularly interesting, and Oluf Borch, whose biography constitutes a separate portion of the monograph, is a native of Jutland and a matriculate of Copenhagen and is given credit for publishing the first report of a case. In the succeeding chapters the author has collected and analyzed 197 cases from the literature and added six additional cases of his own. The conclusion at which he arrives from this analysis is that "if symptoms of cardiac disease occur shortly after a nonpenetrating trauma of the chest or even later (as a rule within a year) there is always a possibility that the pericardium or myocardium has been injured, causing subacute and chronic disease." One must agree with this statement and with his further plea that those hospital departments which receive a fair number of patients with traumatic lesions of the thorax should make a special effort to examine them systematically every day or every other day by physical examination, electrocardiography and x-ray photography. This monograph can be heartily recommended to any practitioner who may be confronted with a problem of this type.

A Text-Book of Pathology: An Introduction to Medicine. By William Boyd, M.D., LL.D., M.R.C.P., Professor of Pathology and Bacteriology in the University of Toronto, Toronto. Third edition. Cloth. Price, \$10. Pp. 1,064, with 475 illustrations. Philadelphia: Lea & Febiger, 1938.

The first edition was published in 1932 and contained 906 pages and 287 illustrations; the third edition, with 1,064 pages, 459 illustrations and sixteen colored plates is an indication of the popularity of this textbook among medical students. As stated in the preface of the first edition, it is written with a single purpose, namely to enable the student to "gain a grasp of the fundamental principles of the subject" without dissipation of his energy in "intriguing rareties or the newest notion of the moment." Numerous paragraphs—in small type in the new edition—on the "relation of symptoms to lesions" demonstrates the "practical" value of pathology in diagnosis. The author's literary style is clear and concise, and by the use of apt allusions and deft turns of phrase the subject of pathology is made interesting, one might almost say entertaining. In addition to the increased number of illustrations, a mass of new material has been added. A section on sudden death is included for the first time. The anemias and pneumonias have been reclassified. The general discussion of viruses has been rewritten, and the virus diseases of the nervous system have been grouped in a manner to emphasize their relation to one another. Much new material is introduced into the various sections. The more important of these additions deal with experimental pulmonary embolism, direct observation of repair in living tissue, the method of bacterial invasion in typhoid, regional ileitis, the pathogenesis of acute pancreatitis and the life cycle of the Aschoff body. The inclusion of the results of recent investigations of inflammation, streptococci, the female sex organs and tumors add much to the corresponding sections. The rearrange-

ment of various chapters is of interest. The first edition opened with the chapter on inflammation, which the author then believed "forms the best starting point for the study of pathology as a whole." In this edition the subject of inflammation is relegated to chapter iv after the discussion of degenerative processes and circulatory disturbances. This is a more logical position. The author's presentation of pathology is frankly dogmatic. This method has certain virtues in a textbook for students. The known or established facts are presented; the uncertainties, while not ignored, are not emphasized. In determining the validity of facts for this purpose there may be differences of opinion. The author still accepts the explanation of Blake and Cecil of the pathogenesis of pneumonia. A single sentence is devoted to the work and opinion of Robertson, while the confirmatory experiments of Gunn and Nungester are not mentioned. While written primarily for medical students, this will prove useful to older practitioners of medicine and surgery. It presents pathology from the modern point of view in relation to the living patient. Any physician will find it a pleasant means of indulging "in the periodic brain dusting recommended by Osler."

Bolezni ucha, nasa i garla: Rukavodstvo diya vrachey. V. trekh tomakh. Tom pervy: Bolezni ucha. Chast vtoraya. Pod redaktsey S. M. Kompaneetsa i A. A. Skrypta. [Diseases of Ear, Nose and Throat: Handbook for Physicians. Volume I: Diseases of Ear. Part 2. Cloth. Pp. 1,542, with illustrations. Kler: Gosudarstvennoe Meditsinskoe Izdatelstvo USSR, 1937.

This is a voluminous work participated in by a large number of contributors under the editorship of S. M. Kompaneets. It is quite exhaustive, covering the field in all its aspects. A particularly commendable feature of the work is to be seen in its attention to the historical development of the specialty as well as a scholarly orientation in the universal literature of this field. A particularly interesting chapter is one dealing with otoneurologic syndromes accompanying the diseases of the central nervous system.

Erscheinungsformen der tuberkulösen Ersterkrankung der Lunge im späteren Schul- und Jugendlichenalter. Von Dr. med. H. Brügger, Direktor der Kinderheilstätte Wangen im Allgäu. Nr. 66, Tuberkulose-Bibliothek, Beihefte zur Zeitschrift für Tuberkulose. Herausgegeben von Dr. Franz Redeker, Oberregierungs- u. Obermedizinalrat, Berlin, und Dr. Karl Diehl, dirigierender Arzt, Sommerfeld. Paper. Price, 7.20 marks. Pp. 34, with 46 illustrations. Leipzig: Johann Ambrosius Barth, 1938.

The illustrations are made from roentgenograms of the chests of older children and young adults. The author presents seventeen cases which have been carefully observed. He finds that a knowledge of the time when the individual first reacts to the tuberculin test is of the greatest importance in proving the development of first infection. In fourteen of his cases the first infection was found to follow precisely the same course in older children and young adults as in younger children; therefore he finds no special danger for those who are first infected in later life. He points out that if one depends for proof of first infection in later life on serial x-ray films only a few cases are proved. A series of tuberculin tests is necessary in the older ages; for example, on entrance into industry.

Der klinische Blick. Von Dr. Erwin Rlsak, Privatdozent für innere Medizin der Universität zu Wien. Second edition. Paper. Price, 6.60 marks. Pp. 226. Vienna: Julius Springer, 1938.

The author emphasizes the value of systematic and well trained clinical observation and points out that an observer will frequently be led by an apparently trivial finding to a correct diagnosis. The book is divided into three parts: A short discussion of the physician's physical senses, the information which may be gathered from the sickroom, and a more comprehensive presentation of what may be learned from the patient himself by physical examination, particularly inspection. The material is the fruit of the author's personal experience and of his contacts with his teachers and older practitioners. There are several defects in this volume, the most serious being overstatement and lack of balanced perspective. The seasoned clinician will be loath to agree with the author that a mere glance is sometimes sufficient to recognize early pregnancy before the patient has disrobed for examination and before she herself is aware of her condition. Nor is it easy to believe that feminine traits are frequently found in chronically constipated males.

Still more questionable is the example of a patient with a so-called thyrotoxic habitus who was warned by the author to refrain from using iodine. She continued in an apparently satisfactory condition until iodine was applied to her skin for some minor procedure. The result of this application of iodine was precipitation of fatal thyrotoxicosis. The experienced clinician can glean interesting information and different points of view but this is hardly a book to be recommended to any one who is not a discriminating reader.

Die Grundlagen der neuzeitlichen Tuberkulosetherapie im Rahmen der allgemeinen Therapie innerer Erkrankungen. Von Dr. med. habil. Werner Hoffmann, Chefarzt der Abteilung für Innere- und Nervenkrankheiten am Stadtkrankenhaus Brandenburg a. d. Havel. Mit einem Geleitwort von Dr. G. Schröder. Nr. 65, Tuberkulose-Bibliothek. Beihefte zur Zeitschrift für Tuberkulose. Herausgegeben von Dr. Franz Redeker und Dr. Karl Diehl. Paper. Price, 9 marks. Pp. 100. Leipzig: Johann Ambrosius Barth, 1937.

The author discusses the treatment of tuberculosis in comparison with the development of medicine as a whole and divides tuberculosis therapy into five stages: (1) therapeutic methods on the basis of organic pathologic studies of the morbid course; (2) therapeutic methods on the basis of a single cause; (3) therapeutic methods on the basis of a pathologic-physiologic method of consideration; (4) the influence on tuberculosis therapy of functional-pathologic methods of consideration; (5) social and psychologic therapy of the tuberculous. This work has a bibliography but there are no illustrations. The presentation is a very general one and does not contain any particularly new material.

The Technique of Contraception: An Outline. By Eric M. Matsner, M.D. Foreword by Frederick C. Holden, M.D. Published for the National Medical Council on Birth Control, 501 Madison Avenue, New York. Fourth edition. Paper. Grátis. Distributed by the National Medical Council on Birth Control to Physicians only. Pp. 50, with 25 illustrations. Baltimore: Williams & Wilkins Company, 1938.

This is a pamphlet containing in rather concise form a statement concerning the most practical methods of contraception. The authors suggest for therapeutic contraception the prescribing of a mechanical barrier—a vaginal occlusive diaphragm (or cervical cap) to be used in conjunction with a spermicidal jelly or cream. It is pointed out that the method is not applicable to all cases. Alternative methods, when indicated, are generally those whereby spermicidal jelly is applied by means of a suitable applicator or the use of a condom.

Insulin: Its Production, Purification and Physiological Action. By Douglas W. Hill, B.Sc., Ph.D., and Frederick O. Howitt, M.Sc., Ph.D., F.I.C. Foreword by Professor E. C. Dadds. Cloth. Price, \$5. Pp. 219, with 7 illustrations. New York: Chemical Publishing Co., of N. Y., Inc., [n. d.].

The English edition of this useful monograph was reviewed in *THE JOURNAL*, July 11, 1936. The work includes chapters on the pathologic physiology of diabetes mellitus, preliminary attempts to isolate the pancreatic hormone, preparation of insulin, purification of insulin preparations, the physical and chemical properties of insulin, the physiologic properties of insulin, the mode of action of insulin, the standardization of insulin preparations, and possible substitutes for insulin, with an extensive bibliography at the end of each chapter. Because of the vast amount of work which is constantly under way in the field of carbohydrate metabolism, any monograph such as this soon becomes out of date. This is strikingly evident in the book under discussion. It was published just at the time when protamine insulin and other slowly acting preparations were being introduced and a new edition would already seem desirable.

A Textbook of General Bacteriology. By Edwin O. Jordan, Ph.D. Revised by William Burrows, Ph.D., Assistant Professor of Bacteriology in the University of Chicago. Twelfth edition. Cloth. Price, \$6. Pp. 808, with 197 illustrations. Philadelphia & London: W. B. Saunders Company, 1938.

Since the previous edition of this work the original author, Professor Jordan, has died. In the revision no essential change has been made in the organization of the book. The sections on oxygen supply and respiration, filtration and isolation of bacteria in pure culture have been rewritten. Extensive revision has been given to the part on viruses. The chapter on pathogenic protozoa has been brought down to date. This book is widely known.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Medical Practice Acts: Treatment with Herbs Constitutes the Practice of Medicine.—The state of Washington instituted proceedings in the superior court, King County, against the defendant Low, charging him with practicing medicine without a license, in violation of the state medical practice act, in that he "wilfully and unlawfully did practice and hold himself out as practicing medicine in this, that he . . . did treat and pretend to treat and heal one Pat Hughes for disease and physical condition, to-wit: by the use of drugs, medical preparations." Low was convicted and appealed to the Supreme Court of Washington.

At the trial, over Low's objection, copies of newspaper advertisements of the Sing Herb Company, which designated Low as the "Directing Herbalist" and announced free consultation and certain office hours, were admitted in evidence. The advertisements stated that "No matter with what you are afflicted, our wonderful herb treatment will positively relieve diseases," naming some twenty-nine diseases or complaints, and that "all disorders disappear without operation." The advertising account was carried in the name of the "Sing Herb Company, by H. S. Low." An investigator for the state testified at the trial that when he visited the address stated in the advertisements Low was referred to by himself and by an office girl as "the doctor." Low, after asking the investigator what ailed him and being informed that he had had a paralytic stroke, advised him to follow a diet set forth on a diet sheet which he gave him. Low also gave him two bottles of "medicine," which had typewritten directions on their labels, and advised him to take the entire contents of one bottle at once. The price for the medicine was to be \$10 a week. Low assured the investigator that the "medicine" would help him if he followed directions and returned.

The Supreme Court could not agree with Low's contention that the superior court had erred in admitting in evidence the newspaper advertisements. In its opinion the investigator's testimony showed that Low was connected with the Sing Herb Company, so that the advertisements, which would otherwise have been inadmissible in evidence because no foundation had been laid for their introduction, were admissible to prove that the defendant was engaged in that particular character of practice of medicine which the state charged him with practicing. Likewise, the court was unable to agree with Low's further contention that the evidence was insufficient to sustain the conviction. It was undisputed that Low had called himself "the doctor." Certain of the advertisements announced "consultation free" and all of them emphasized that "our wonderful herb treatment will positively relieve" practically every disease of which medical science has any knowledge. Low diagnosed the case of the investigator to the extent of prescribing some liquid. What that liquid was made no difference and therefore it was not necessary for the state to have an analysis made of it. The court called attention to the fact that Low did not hold a license to practice any branch of the healing art and specifically stated that the question of whether an analysis of the "medicine" would be material if Low were licensed to practice in one of the restricted fields of the healing art was not before the court. In the judgment of the court, Low had held himself out as practicing medicine, without a license so to do.

Furthermore, the court was of the opinion that the superior court had not erred, as Low contended, when it incorporated in its instruction as to the meaning of the term "drug" only the last portion of the statutory definition set forth in the food and drug law of the state, which provides:

"The term 'drug,' as used in this act, shall include all medicines and preparations recognized in the United States Pharmacopoeia or National Formulary for internal or external use, and any substance or mixture of substances intended to be used for the cure, mitigation or prevention of disease of either man or other animals." [Italics supplied by court.]

Only the latter portion of the statutory definition, said the court, was applicable to the facts in the present case.

The Supreme Court affirmed Low's conviction but it reversed the judgment and remanded the case for resentencing because the superior court had erred when it imposed a penalty of both fine and imprisonment when the statute authorized only fine or imprisonment.

In a special dissenting opinion, Chief Justice Steinert disagreed with the affirmation of Low's conviction, because, in his opinion, the copies of the newspaper advertisements were inadmissible in evidence and the state had failed to prove the charge in its complaint that Low had treated the supposed patient "by the use of drugs, medical preparations." The evidence showed only that Low supplied the investigator with a diet sheet and two bottles containing "herbs." No chemical analysis of the contents of the bottles was made. It was not shown, therefore, according to this dissenting opinion, that the "herbs" consisted of or contained drugs or medicinal preparations, and it cannot be presumed that they did. The chief justice also was of the opinion that the superior court, by limiting without qualification its definition of the term "drug" to the latter part of the statutory definition, gave the jury to understand that any substance or mixture of substances used as a cure or prevention of disease was a "drug." As thus defined the word "drug" would apply equally to any article of food or drink no matter how innocuous it might be. Under such a construction of the meaning of the term "drug," any one who should treat disease by a food diet or any form of drugless healing would be practicing medicine. In his opinion such a construction was untenable.—*State v. Low* (Wash.), 74 P. (2d) 458.

Workmen's Compensation Acts: Compensability of Death Following Inhalation of Ammonia.—On the morning of Feb. 10, 1935, Holmes, an engineer employed in the refrigerating plant of the defendant, was found lying on the floor a short distance from a broken pipe from which ammonia gas had escaped. After he had been carried outside and a gas mask he was wearing had been removed, he vomited. When he arrived at his home he had difficulty in breathing and coughed frequently. Later, to aid his breathing, it was necessary to prop him up with pillows. His appetite failed, he did not sleep well and his condition became progressively worse. He had to quit work on March 26, about which date he entered a hospital, but he returned home three weeks later. A few weeks thereafter he entered another hospital and there he developed pneumonia and died. The claimant, his wife, brought proceedings under the workmen's compensation act of Illinois against the employer. From a judgment of the superior court of Cook County affirming an award of the industrial commission in her favor, the company appealed to the Supreme Court of Illinois.

According to the record, except for a short illness in October 1934 Holmes had been in good health prior to the accident. A physician who treated him sometime after the accident in February 1935 testified that when he was summoned in the latter part of March 1935 Holmes had a bad bronchitis, a bad heart and diseased kidneys. He testified further that ammonia gas attacks the mucous membranes, causes irritation in the respiratory organs and results in a toxic condition. The coroner, a physician who had performed an autopsy on Holmes's body, testified that death was not due to the exposure to ammonia fumes. He was of the opinion that Holmes's heart, kidneys, bladder, prostate and spleen were diseased and that these conditions, together with the pneumonia, had caused death. The coroner, however, admitted that evidence that Holmes had been almost suffocated by ammonia so that he gasped for breath and was "knocked out" would make a difference in his opinion as to the causal connection between the exposure to ammonia gas and death. Another physician, in answer to a hypothetical question, testified that a causal connection existed between the exposure to ammonia gas and the subsequent condition of ill-being and death. In his opinion, the coughing, gasping and choking that appeared after exposure to the ammonia fumes were due to his heart condition as well as to the exposure to the fumes. He testified further that "an infection will result from exposure to ammonia and that the weakened condition of the person thus infected may result in such further infections as those Holmes was shown to have had in his urinary organs."

The findings of the industrial commission on contested issues of facts, said the Supreme Court, will not be set aside on appeal

unless they are manifestly against the weight of the evidence. In the judgment of the court, it had been shown by competent evidence that Holmes had been exposed to free anhydrous ammonia, a dangerous gas, and that he was overcome and "knocked out" by the fumes. The court concluded that there was substantial evidence from which the industrial commission was justified in finding that Holmes sustained an accidental injury which arose out of and in the course of his employment and which later caused his death. Accordingly, the Supreme Court affirmed the judgment in favor of the claimant.—*Armour & Co. v. Industrial Commission* (Ill.), 11 N. E. (2d) 949.

When a Corporation Is Not Liable on Promise to Pay Hospital Bill.—Oddson, who had been at one time an employee of the defendant corporation, the Mackie Mill Company, was refused admission to a hospital in Seattle unless the hospital was paid in advance for its services. The president of the corporation wrote to the hospital that the corporation would pay Oddson's hospital expenses. Oddson was then admitted and cared for. The corporation, however, subsequently refused to pay the hospital for the services that it had rendered. The hospital then assigned to the plaintiff in the present case its claim against the corporation and he brought suit. The defendant corporation contended that its promise to pay could not be enforced against it, because that promise was ultra vires; that is, beyond the power of the corporation to make. The corporation contended that it was incorporated as a trading and manufacturing corporation and had no authority to become a surety or a guarantor of the debts of others. The trial court held that, although the promise to pay was ultra vires, the corporation was estopped from asserting that defense and entered a judgment in favor of the plaintiff. The corporation thereupon appealed to the Supreme Court of Washington.

The Supreme Court, with four judges dissenting, reversed the judgment of the trial court and ordered the case dismissed. The defense of ultra vires, said the Supreme Court, is not available to a corporation that has received, directly or indirectly, the benefits of an ultra vires contract, but if the corporation has received no benefits from the performance of such a contract it is not estopped from pleading that the contract was one beyond the power of the corporation to make. In this case the corporation received no benefit from the contract that it had made, involving the rendering of hospital care to a former employee. "To adopt a rule," said the court, "that would not allow the ultra vires defense would endanger the investments and savings of thousands of large and small investors who either own stock or bonds of a corporation. Such a rule would leave it in the power of managers or officers of large and small corporations to destroy the business of such corporations by making improvident contracts contrary to the business for which they were incorporated." The Supreme Court concluded that the contract signed by the president of the corporation was ultra vires, that the defense of ultra vires was available and that the corporation was not responsible for the guaranty.—*Millett v. Mackie Mill Co.* (Wash.), 76 P. (2d) 311.

Society Proceedings

COMING MEETINGS

- American Society of Tropical Medicine, Oklahoma City, Nov. 15-18.
- Dr. E. Harold Hinman, Wilson Dam, Ala., Secretary.
- American Student Health Association, New York, Dec. 29-30. Dr. Ruth E. Boynton, Students Health Service, University of Minnesota, Minneapolis, Secretary.
- Pacific Coast Society of Obstetrics and Gynecology, Los Angeles, Nov. 30-Dec. 3. Dr. T. Floyd Bell, 400 29th St., Oakland, Calif., Secretary.
- Radiological Society of North America, Pittsburgh, Nov. 28-Dec. 2. Dr. Donald S. Childs, 607 Medical Arts Bldg., Syracuse, N. Y., Secretary.
- Society for the Study of Asthma and Allied Conditions, New York, Dec. 3.
- Dr. W. C. Spain, 116 East 53d St., New York, Secretary.
- Society of American Bacteriologists, New Haven, Conn., Dec. 28-30. Dr. I. L. Baldwin, Agricultural Hall, University of Wisconsin, Madison, Wis., Secretary.
- Southern Medical Association, Oklahoma City, Nov. 15-18. Mr. C. P. Loran, Empire Bldg., Birmingham, Ala., Secretary.
- Southern Surgical Association, White Sulphur Springs, W. Va., Dec. 6-8.
- Dr. Alton Ochsner, 1430 Tulane Ave., New Orleans, Secretary.
- Western Surgical Association, Omaha, Dec. 2-3. Dr. Albert H. Montgomery, 122 South Michigan Blvd., Chicago, Secretary.

Current Medical Literature

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Titles marked with an asterisk (*) are abstracted below.

American Heart Journal, St. Louis

16: 261-388 (Sept.) 1938

Effect of Excess Sugars on Perfused Rabbit Heart. A. J. Geiger and W. E. Hambourger, New Haven, Conn.—p. 261.

Hemodynamic Studies in Experimental Coronary Occlusion: V. Changes in Arterial Blood Pressure. L. Gross, G. Schauer and M. Mendlowitz, New York.—p. 278.

Bundle Branch and Intraventricular Block in Acute Coronary Artery Occlusion. A. M. Master, S. Dack and H. L. Jaffe, New York.—p. 285.

Form of Electrocardiogram in Experimental Myocardial Infarction: V. Later Effects Produced by Ligation of Right Coronary Artery. I. G. W. Hill, F. D. Johnston and F. N. Wilson, Ann Arbor, Mich.—p. 309.

Cardiac Output in Arterial Hypertension: Part II. Study of Arterial Hypertension Produced by Constricting Renal Arteries in Unanesthetized and Anesthetized (Pentobarbital) Dogs. D. V. Holman and I. H. Page, New York.—p. 321.

Human Autonomic Pharmacology: XVIII. Effects of Intra-Arterial Injection of Acetylcholine, Acetyl-Beta-Methylcholine Chloride, Epinephrine and Benzedrine Sulfate. A. Myerson, J. Loman, M. Riinkel and M. F. Leszes, Boston.—p. 329.

*Clinical Significance of Persistent Depression of RS-T Segment in Electrocardiogram. A. Selzer, London, England.—p. 336.

Further Observations on Apical Systolic Murmurs in Children. L. G. Steuer and M. H. Fineberg, Cleveland.—p. 351.

Pancreatic Necrosis Associated with Auricular Fibrillation and Flutter: Report of Case Simulating Coronary Thrombosis (Autopsy Findings). E. L. Dittler and T. H. McGavack, New York.—p. 354.

Significance of Depression of RS-T Segment.—Selzer examined 2,000 electrocardiographic curves taken in routine work in order to discover the incidence of a permanent depression of the RS-T segment. The electrocardiograms of 150 healthy persons between 15 and 40 years of age were also examined. It was found that both in the standard and in the chest leads the RS-T segment was almost invariably isoelectric. In the 2,000 electrocardiograms there were 178 instances in which a persistent depression of the RS-T segment was present. In fifty-six of these the depression was due to digitalis, and these records were excluded from further study. In the remaining 122 cases hypertensive cardiac disease was found responsible in sixty-nine, syphilitic aortic valvular disease in nineteen, non-syphilitic aortic valvular disease in eight, coronary artery disease in seven, rheumatic mitral valvular disease in nine, cor pulmonale in four, congenital cardiac disease in one, infective endocarditis in one, myxedema in two and thyrotoxicosis in two. These figures reveal that a depression of the RS-T segment may occur in all types of cardiac disease, the distribution of cases corresponding roughly to the frequency of the disease in the material examined. The statement of many German authors that the depression of the RS-T segment is a specific sign of coronary insufficiency was not confirmed.

American Journal of Medical Jurisprudence, Boston

1: 1-72 (Sept.) 1938

The Medical Man on the Witness Stand. E. O'Dunne, Baltimore.—p. 1.

Blood Groups in Disputed Paternity. M. Pijoan, Boston.—p. 5.

What Constitutes Body Attack in Medical Practice? H. V. Barbour, Detroit.—p. 9.

The Expert Witness and the Insanity Defense Plea. M. H. Hoffmann, Dearborn, Mich.—p. 12.

Interpretation of X-Rays in Court Hearings. L. H. Garland, San Francisco.—p. 19.

Organized Society's Interest in Death. O. T. Schultz, Evanston, Ill.—p. 22.

Detailed Examination Required to Determine Whether Rape Has Been Committed. J. R. Garner, Atlanta, Ga.—p. 29.

Doctors, Juries and Judgments. P. E. Craig, Coffeyville, Kan.—p. 32.

Diagnosis and Treatment of Legal Congestion. A. Koerner, New York.—p. 34.

American Journal of Medical Sciences, Philadelphia

196: 461-608 (Oct.) 1938

*Mental Symptoms of Pellagra: Their Relief with Nicotinic Acid. T. D. Spies, C. D. Aring, J. Gelperin and W. B. Bean, Cincinnati.—p. 461.

*Studies in Alcohol: I. Diagnosis of Acute Alcoholic Intoxication by Correlation of Clinical and Chemical Findings. W. W. Jetter, Buffalo.—p. 475.

Id.: II. Experimental Feeding of Alcohol to Nonalcoholic Individuals. W. W. Jetter, Buffalo.—p. 487.

Red Cell Mass in Polycythemia in Relation to Diagnosis and Treatment. R. L. Haden, Cleveland.—p. 493.

*Use of Mapharsen in Treatment of Malaria. D. Goldman, Cincinnati.—p. 502.

Use of 2 (*p*-Aminobenzenesulfonamido) Pyridine in Treatment of Pneumonia: Preliminary Report. H. F. Flippin and D. S. Pepper, Philadelphia.—p. 509.

Partial and Complete Heart Block in Acute Coronary Artery Occlusion. A. M. Master, S. Dack and H. L. Jaffe, New York.—p. 513.

Kidney Function and Uremia in Renal Amyloidosis. M. F. Mark and H. O. Mosenthal, Staten Island, N. Y.—p. 529.

Diabetes Insipidus with Big Bladder (Capacity Two Liters). E. Rixford and H. Gray, San Francisco.—p. 540.

Syndrome Consisting of Affections of Kidney, Stunted Growth, Rickets and Disturbed Cystine Metabolism. G. O. E. Lignac, Leiden, Netherlands.—p. 542.

Study of Silicosis. P. B. Matz, Washington, D. C.—p. 548.

Contralateral Spontaneous Pneumothorax Complicating Artificial Pneumothorax: Report of Two Cases. J. B. Andosca, Boston.—p. 559.

Role of Cervical Nerves in Facial Sensations and Quantitative Disturbance of Sensitivity in Major Trigeminal Neuralgia. F. H. Lewy, Philadelphia.—p. 564.

Pathologic Considerations of Thoracic Duct. R. N. Washburn, Rochester, Minn.—p. 572.

Mental Symptoms of Pellagra.—Spies and his colleagues observed sixty pellagrins with acute psychoses and other manifestations of pellagra, fifteen other pellagrins with no mental symptoms but with characteristic dermatitis, glossitis, stomatitis and gastrointestinal involvement, 424 patients with subclinical and mild pellagra who have been subject to one or two annual recurrences of the disease, twenty-six patients with psychoses of other types and 129 pellagrins who had had one or two recurrences of their "neurotic" symptoms each "pellagra season" since the onset of their disease. Patients with subclinical pellagra are noted for the multiplicity of their complaints, among which are many that are usually classified as neurasthenic. The most common of these symptoms are fatigue, insomnia, anorexia, vertigo, burning sensations in various parts of the body, numbness, palpitation, nervousness, a feeling of unrest and anxiety, headache, forgetfulness, apprehension and distractibility. The conduct of the pellagrin may be normal; but he feels incapable of mental or physical effort, even though he may be ambulatory. The studies suggest that nicotinic acid in adequate amounts is a specific therapeutic agent for the acute mental symptoms of pellagra. Both spontaneous and induced psychoses of pellagra respond promptly to this therapy. Coramine, the diethyl amide of nicotinic acid, also is beneficial in the treatment of the abnormal mental symptoms. The psychoses present in twenty-six non-pellagrous persons did not improve after the ingestion of these drugs. The so-called prodromal or neurotic symptoms of pellagra usually disappear following the administration of nicotinic acid. The studies were conducted in such a manner that suggestion was eliminated, and they indicate that the vague, subjective, prodromal symptoms are evidence of disordered function. Frequently repeated large doses of nicotinic acid prevent the development of mental symptoms in patients with subclinical and with mild pellagra. The minimal dose of nicotinic acid has not been determined but seems to vary from case to case. It is tentatively recommended that each patient with severe mental symptoms receive a total of at least 500 mg. daily. It is preferable to give this in ten doses. In the extremely severe cases convalescence seems to be shortened by the administration of 1,000 mg. daily. Since nicotinic acid is only one of the essential chemical substances present in the well balanced diet, all patients with pellagra should be given a well balanced diet whenever possible, even though nicotinic acid is used as a supplement.

Acute Alcoholic Intoxication.—In order to correlate the clinical observations of acute alcoholism with the concentration of alcohol in the blood and urine, Jetter studied 1,159 patients admitted to the Buffalo City Hospital with a diagnosis of acute alcoholism. The alcohol content of the blood and urine was determined by the method devised by Heise in 1934. Definite criteria were adopted for the clinical diagnosis of acute alcohol-

ism. Abnormality in gait was required as an absolutely essential finding in association with any two of four other changes: abnormality of speech, alcoholic odor of breath, flushed face and dilated pupils. In the determination of incoordination of locomotion, gross swaying, staggering or reeling must be present. Blood was obtained for analysis from 1,150 patients; 1,000 were alcohol positive and 150 alcohol free. In 372 of the 1,000 subjects showing alcohol in the blood, the urine was also obtained for analysis. Of the 150 individuals who were free of alcohol at admission, seventy-eight were known chronic alcoholic addicts. Various conditions may be confused with acute alcoholism particularly if the patient is comatose, which condition was present in thirty-seven cases. Of these, sixteen resulted from overdosage of either paraldehyde or barbitol derivatives, while diabetes mellitus, uremia, cerebral injuries, cardiovascular accidents and schizophrenia accounted for nearly all others. The remaining thirty-five, occurring in nonalcoholic persons, were admitted in a noncomatose condition. An alcoholic odor was present in 903 of the 1,000 patients. Abnormalities of gait and speech were found in 750 and 721 cases, respectively. In most instances, abnormality of speech accompanied an abnormality of gait. The incidence of dilated pupils closely followed, occurring in 713 cases, while that of flushed face was lowest with a total of 606 cases. Alcohol was found in the urine of 381 persons, all but nine of whom were included in the group of 1,000 cases showing alcohol in the blood. An analysis of the 1,000 cases showing alcohol in the blood was made with regard to the occurrence of clinical criteria at the various alcoholic concentrations. With an alcohol concentration of from 0.05 and 0.1 per cent, abnormalities of both gait and speech were present in less than 20 per cent of the cases, at 0.15 per cent the percentage was approximately 40 and at 0.2 per cent approximately 80. The percentages gradually approached 100, which occurred in the group with a concentration of 0.45 per cent of alcohol. In most instances, abnormality of gait occurred slightly more frequently than did abnormality of speech. The incidence of alcoholic odor was high at all concentrations of alcohol, never dropping lower than 73 per cent at group 0.05 per cent of alcohol. The incidence of dilated pupils and flushed face did not follow the curve representing the incidence of clinical intoxication. While the incidence of both these criteria rose somewhat with increasing concentrations of alcohol (approximately 80 per cent in groups 0.3 and 0.35 per cent of alcohol), their percentage occurrence decreased with still higher levels. Of the 381 cases showing a positive test for alcohol in the urine, 372 were included in the 1,000 cases in which alcohol was found in the blood. No instances were observed with urine positive for alcohol and the blood negative or vice versa. The urinary concentration of alcohol was usually higher than that in the blood. The average ratio of the alcoholic concentration of the blood and urine in these 372 cases was blood to urine as 1:1.23. No person showed a concentration above 0.5 per cent of alcohol in the urine. An analysis of the urine series in respect to the occurrence of clinical criteria at various groups of alcohol concentration closely follow the incidence of clinical intoxication.

Mapharsen in Malaria.—Goldman began to use mapharsen in the treatment of therapeutic malaria in 1937. He also used it in a naturally occurring case of chronically recurring malaria of about eight months' standing. Its administration in malaria differs in no way from that used in syphilis. In most cases (more than 90 per cent of twenty-four cases), a single injection suffices to terminate the malaria permanently, but to obviate recurrences it is well to give three or four injections at the proper intervals. In therapeutic malaria as usually employed for dementia paralytica a course of from eight to ten injections will usually be given for the sake of its antisiphilitic value and at the same time the malaria is permanently eradicated. Mapharsen has been found to be much less toxic in debilitated patients than neoarsphenamine or even quinine. It also seems safer to use than atabrine. No toxic manifestations have occurred. Even malaria associated with severe leukopenia responded favorably and with an increase in the leukocytes. Recurrences after mapharsen are rare and are encountered only in severe cases which in this series (two) were believed to have been allowed to run longer than was advisable. The disappearance of the parasites is almost immediate. After twenty-four hours it is only rarely that a disintegrating form can be

found in the blood smears. Splenomegaly begins to disappear almost as rapidly. Usually within a day the spleen is appreciably smaller and within three or four days it has receded behind the costal margin. If a chill is to be expected in less than twenty-four hours it usually occurs in spite of the injection, but if the chill is not due for more than twenty-four hours or if the injection is given at the height of a chill no subsequent chill will occur. The efficacy of mapharsen has not been observed in estivo-autumnal malaria. It is most important to determine what effect if any it will have on the notoriously resistant gametocytes of malignant malaria.

American Journal of Public Health, New York

28: 1153-1268 (Oct.) 1938

- Sylvatic Plague. K. F. Meyer, San Francisco.—p. 1153.
Contributions of Edward Jenner to Modern Concepts of Heart Disease. O. F. Hedley, Philadelphia.—p. 1165.
*Alum Precipitated Toxoid for Prevention of Diphtheria. A. S. Dean and S. Hyman, Buffalo.—p. 1170.
Present Status of Safety Education in Some Representative School Systems. J. P. Sullivan, Boston.—p. 1175.
Registration and Approval of Public Health Laboratories as Carried on in Connecticut. F. L. Mickle, Hartford, Conn.—p. 1185.
Development of International Cooperation Among the Health Authorities of the American Republics. H. S. Cumming, Washington, D. C.—p. 1193.
Positions and Rates of Pay in Public Health Agencies. A. J. Borowski, Washington, D. C.—p. 1197.
Trichinelliasis in San Francisco. M. Hobmaier and J. C. Geiger, San Francisco.—p. 1203.
Epidemic of Typhoid Fever Attributed to Salad Contaminated by Chronic Typhoid Carrier. P. A. Lembecke and P. Von Haesseler, Albany, N. Y.—p. 1212.
Dye Concentration in Culture Mediums Employed for Analysis of Escherichia-Aerobacter Members in Milk. H. D. McAuliffe and M. A. Farrell, State College, Pa.—p. 1217.
Bovine Mastitis: Relation of Streptococci to Physical Changes Occurring in the Udders of Dairy Cows. W. T. Miller and H. W. Johnson, Beltsville, Md.—p. 1222.
Inexpensive Method for Dehydration and Preservation of Complement and Other Biologic Materials. E. E. Ecker and L. Pillemer, Cleveland.—p. 1231.
Educational Qualifications of Subprofessional Field Personnel in Sanitation. W. S. Leathers, Nashville, Tenn.—p. 1233.

Prevention of Diphtheria.—Alum precipitated toxoid (meeting the standards of the National Institute of Health) was administered to 620 persons, of whom 442 were Schick positive and 178 had not been given the Schick test. Dean and Hyman state that one dose of 1 cc. of the material was injected subcutaneously on the outer upper part of the left arm. A nodule remained in the arm usually for weeks, but no undue reactions or abscesses were reported. At four, sixteen and twenty-eight months after the administration of the toxoid, Schick tests were given to as many as possible of the 620 persons who received the product. The procedure was the same as described for the preliminary intracutaneous test of susceptibility to diphtheria toxin. There were 401 persons given the Schick test at four months, 385 at sixteen months and 246 at twenty-eight months. Among 159 who were Schick negative four months after having received 1 cc. of alum precipitated toxoid, 152 remained negative twenty-eight months after they obtained the toxoid. The percentage is nearly as high, 94, among sixty-nine persons who were known to be Schick positive prior to the receipt of the precipitated toxoid and to have had no previous toxoid or toxin-antitoxin. Among seven persons Schick positive four months after receipt of 1 cc. of alum precipitated toxoid, five were Schick negative twenty-eight months after the injection of the toxoid. The results of the intracutaneous tests of susceptibility to diphtheria showed that at the end of four months from the receipt of the toxoid 175 of 204 of the persons tested were Schick negative, at the end of sixteen months 162 of 187 persons were Schick negative, and at the end of twenty-eight months ninety-eight of 110 persons were Schick negative. The increasing immunity with the lapse of time may be due partly to the late effects of the alum precipitated toxoid to Schick test toxin or to naturally acquired immunity. Of 140 Schick positive persons unsuccessfully treated with unmodified toxoid or toxin-antitoxin, 94, 90 and 98 per cent were Schick negative four, sixteen and twenty-eight months after receiving alum precipitated toxoid. The administration of alum precipitated toxoid to 178 persons who had not previously been given the Schick test and had not formerly received toxoid or toxin-antitoxin gave

Schick negative responses four, sixteen and twenty-eight months of 98, 98 and 95 per cent. Thirty-seven per cent of 466 persons in an epidemic area who had never had toxoid or toxin-antitoxin were found Schick negative.

American Review of Tuberculosis, New York

38: 399-530 (Oct.) 1938

- Molecular Weight, Electrochemical and Biologic Properties of Tuberculin Protein and Polysaccharide Molecules. Florence B. Seibert, Philadelphia; K. O. Pedersen and A. Tiselius, Uppsala, Sweden.—p. 399.
- Incidence and Control of Tuberculosis in High School Children. H. W. Hetherington, H. L. Israel and P. B. Kreitz, Philadelphia.—406.
- Tuberculosis Studies in Tennessee: Roentgenologic Evidence of Tuberculous Infection in Relation to Tuberculin Sensitivity in School Children. R. S. Gass, R. L. Gauld, E. F. Harrison, H. C. Stewart and W. C. Williams, Nashville, Tenn.—p. 441.
- Mass Case-Finding. A. B. Robins, New York.—p. 448.
- Results of Treatment of Tuberculosis in the Negro. G. D. Kettelkamp, P. Murphy and D. Trumpe, St. Louis.—p. 458.
- *Anemia of Pulmonary Tuberculosis. M. M. Braverman, Waltham, Mass.—p. 466.
- Normal Sedimentation Rate in Open Pulmonary Tuberculosis. A. L. Banyai and Esther Caldwell, Wauwatosa, Wis.—p. 491.
- Erythrocyte Sedimentation: Its Practical Value in Ambulatory Tuberculosis Clinic. H. T. Pessar and A. Hurst, New York.—p. 495.
- Culture of Tubercle Bacilli: I. Effect of Sodium Hydroxide and Sulfuric Acid on Acid-Fast Variants of Homologous Strains and Influence of Hydrogen Ion Concentration in Different Mediums on Subsequent Growth. W. Steenken Jr. and M. M. Smith, Trudeau, N. Y.—p. 503.
- Medium for Culture, Isolation and Dissociation of Tubercle Bacilli. W. Steenken Jr. and M. M. Smith, Trudeau, N. Y.—p. 514.
- Tuberculoma of Lumbar Spinal Cord. E. Kupka and R. E. Olsen, Pontiac, Mich.—p. 517.

Anemia of Pulmonary Tuberculosis.—Braverman studied the anemia associated with pulmonary tuberculosis in 509 cases. The venous method of obtaining the blood was used. Sections of bone marrow were obtained from about 100 subjects at thoracoplasty and at necropsy. As the amount and chronicity of the pulmonary disease increase, the number, size and hemoglobin content of the erythrocytes decrease. The incidence of anemia increases to 46 per cent when the mean corpuscular hemoglobin concentration is also taken into account. The most common types of anemia encountered are hypochromia and microcytosis. In the routine care of most tuberculous patients, the correction of the sedimentation rate of the erythrocytes for anemia is not necessary unless the anemia is severe. The icterus index values drop, often close to two units, as the amount and severity of the pulmonary lesion increase. It is believed that there is a partial inhibition of hemoglobin synthesis with an increasing severity of the pulmonary tuberculosis. In the treatment of the anemia associated with pulmonary tuberculosis, ferrous salts are the most effective. It cannot yet be stated statistically that the patients who received iron therapy now have a better prognosis than those who did not. Clinically, the group treated with iron fared better symptomatically than the other group.

Archives of Ophthalmology, Chicago

20: 541-708 (Oct.) 1938

- Physiologic and Clinical Ophthalmologic Problems in Relation to Individual Variability. A. Brückner, Basel, Switzerland.—p. 541.
- *Nature of Filtrable Agent of Trachoma. P. Thygeson, New York, and P. Richards, Albuquerque, N. Mex.—p. 569.
- Evaluation of Homatropine-Benzedrine Cycloplegia. H. F. Sudranski, Indianapolis.—p. 585.
- Cataract Operation to Reduce Incidence of Prolapse of Iris. F. C. Parker, Norristown, Pa.—p. 597.
- Induced Size Effect: I. New Phenomenon in Binocular Space Perception Associated with Relative Sizes of Images of Two Eyes. K. N. Ogle, Hanover, N. H.—p. 604.
- Experimental Iontophoresis of Rabbits' Corneas: Report of Two Cases of Corneal Dystrophy with Treatment by Ionic Medication. S. G. Seech and W. L. Cooper, Los Angeles.—p. 624.
- Inferior Iridotomy in Operations for Cataract on Eyes with Posterior Synechiae or Pupillary Membrane: Value of Operation. P. A. Chandler, Boston.—p. 641.
- Results of Autotransplantation of Cornea into Anterior Chamber: Their Significance Regarding Corneal Nutrition. T. Gundersen, Boston.—p. 645.
- Intern's Experiences with Verhoeff Method of Cataract Extraction. P. H. Case, Phoenix, Ariz.—p. 651.

Nature of Filtrable Agent of Trachoma.—Thygeson and Richards performed twenty-two filtration experiments on human volunteers, monkeys and baboons. Six active filtrates were obtained under conditions designed to insure maximal activity

of the material to be filtered and minimal losses due to adsorption in the filter. Maximal activity of the trachomatous material was attained in five of the six successful experiments by using pooled epithelial scrapings from trachomatous Indian children (selected for activity). For the sixth experiment the material was obtained from an adult white person with acute trachoma. Since the available evidence now indicates that the agent of trachoma has an epithelial localization, the type of material utilized is probably important. The material yielding active filtrates contained substantial numbers of epithelial cell inclusions. On the basis of the observations it is believed that the elementary bodies of trachoma are virus bodies like those of psittacosis and inclusion blennorrhoea and that they are similar, except in staining reactions, to typical virus elementary bodies, such as those of vaccinia, fowlpox and molluscum contagiosum. Belief that the elementary body of trachoma represents the morphologic unit of the virus of trachoma rests, in the authors' opinion, principally on the following observations: (1) the identity in morphologic structure and staining reactions of the bodies of trachoma with the similar bodies of inclusion blennorrhoea and psittacosis, established virus diseases, (2) the presence of the elementary bodies in the lesions of trachoma with sufficient constancy to indicate etiologic significance, (3) the presence of elementary bodies in an infective filtrate, (4) their multiplication in new hosts (man and baboon) when transferred directly or after filtration and (5) their persistence in the lesions of trachoma throughout its period of activity. The elementary body of trachoma has, in their opinion, the essential properties of a virus and should be classified, for the present at least, as a filtrable virus. It does, however, differ from the typical virus elementary body (such as that of vaccinia) in the ease with which it stains and in its regular morphologic variation. In these respects it resembles Rickettsiae, particularly Rickettsia ruminantium of Heartwater.

Archives of Surgery, Chicago

37: 521-696 (Oct.) 1938

- *Pathogenic Bacteria in the Air of Operating Rooms: Their Widespread Distribution and Methods of Control. D. Hart, Durham, N. C.—p. 521.
- Acute Osteomyelitis of Long Bones of Adults. I. Zadek, New York.—p. 531.
- Fibrin Stones: Report of Four Cases. C. D. Allen and J. W. Ragsdale, Memphis, Tenn.—p. 546.
- Malignant Endometriosis of Ovary, Resembling Arrhenoblastoma: Report of Case in a Girl Aged Nineteen. C. R. Tuthill, Staten Island, N. Y.—p. 554.
- Myoblastic Sarcoma of Urinary Bladder. E. F. Hirsch and B. M. Brown, Chicago.—p. 562.
- Dead (Ox) Fascia Grafts in Tendon Defects: Experimental Study. E. D. Weinberg, Baltimore.—p. 570.
- Congenital Anomalies of Genitalia Associated with Unilateral Renal Agenesis, with Particular Reference to True Unicornuate Uterus: Report of Cases and Review of Literature. H. B. Shumacker Jr., New Haven, Conn.—p. 586.
- *Concentration of Procaine in Cerebrospinal Fluid of Human Being After Subarachnoid Injection. H. Koster, A. Shapiro and A. Leikensohn, Brooklyn.—p. 603.
- Effect of Biliary Operations on Liver: Their Relation to Concentration of Bile Acids in Bile. H. K. Gray, W. L. Bultsch and J. M. McGowan, Rochester, Minn.—p. 609.
- Subacromial Bursitis: Clinical, Roentgenographic and Statistical Study. S. R. Rubert, Iowa City.—p. 619.
- Endometriosis of Umbilicus: Vicarious Menstruation Following Hysterectomy. R. Boggs, New York.—p. 642.
- Vaginal Hernia: Review of Literature. W. E. B. Hall, St. Joseph, Mo.—p. 651.
- Review of Urologic Surgery. A. J. Scholl, Los Angeles; F. Hinman, San Francisco; A. von Lichtenberg, Budapest, Hungary; A. B. Hepler, Seattle; R. Gutierrez, New York; G. J. Thompson, J. T. Priestley, Rochester, Minn.; E. Wildbolz, Berne, Switzerland, and V. J. O'Connor, Chicago.—p. 667.

Pathogenic Bacteria in Operating Rooms.—Hart asked fifty surgeons in twenty-five states to make cultures in the operating rooms in which they worked, in order to determine the extent and degree of the bacterial contamination of the air. Reports were received from thirty-two surgeons, covering thirty-seven operating rooms in thirty-three hospitals located in seventeen states. Exclusive of bactericidal irradiation, air conditioning is the most important single means of reducing the bacterial content of the air in the occupied operating room. The organisms in the outside air (predominantly nonpathogenic;

spores, gram-negative bacilli and fungi) are removed by the air conditioning system. The organisms given off in the room by the occupants (predominantly pathogenic; staphylococci and occasionally streptococci) are removed more rapidly by the clean, circulating air from an efficient ventilating system. Other things being equal, the number of pathogenic bacteria in the air of a room increases directly with the number of occupants and the duration of their occupancy. Conversely, the bacterial count drops directly in proportion to the length of time the room is unoccupied and closed. A canopy over the sterile supply tables is of some value in cutting down the contamination of these supplies. Only one report made any reference to the prevalence of infections of the respiratory tract. With four occupants of the operating room suffering from colds, Petri dishes of blood agar exposed for one hour showed an average of 13.8 colonies of streptococci per dish. Only this report stated that an appreciable number of the organisms were in the air. The concentration of *Staphylococcus aureus* in the air of the operating rooms at Duke Hospital is proportional to the number of carriers present. In one hospital during the three weeks covered by the test, with heavy sedimentation of *Staphylococcus aureus* from the air, three wounds were infected with this organism. The total number of colonies of bacteria sedimenting from the air gives some idea of the degree of contamination of the air but is of less significance than the number of pathogenic organisms present. The majority of the pathogenic bacteria reported were staphylococci. In the author's experience more than 90 per cent of infections of wounds are caused by staphylococci. He is convinced that in most cases the infection is caused by dropping of the organisms in the air into the wound or on the sterile supplies that will enter the wound. Streptococci were recovered from the air in relatively small numbers. This may probably be accounted for by the relatively few carriers and the susceptibility of the organism to drying. The organism is probably present in the air of the operating room in large numbers during epidemics of infection of the respiratory tract. Infections of wounds have been traced to carriers of streptococci. During epidemics of influenza the streptococci most likely reach the wound and sterile supplies by way of the air. In the Duke Hospital, by sterilizing the air with bactericidal radiation, it has been possible to get an operative field from which less than one colony to a Petri dish per hour of exposure can be cultured. With this technic, unexplained infections in primary clean incisions have practically disappeared, the postoperative course is smoother, elevated temperatures are less frequent and of shorter duration, the wound is less sore and the general systemic reaction is milder than when radiation is not used.

Procaine in Cerebrospinal Fluid After Injection.—Koster and his associates studied the concentration of procaine hydrochloride in the cerebrospinal fluid of 122 adult patients. Each patient received an injection of 150 mg. of procaine hydrochloride dissolved in 3.5 cc. of cerebrospinal fluid at the interspace between the second and the third lumbar vertebra. The concentration of the anesthetic was determined up to ninety minutes after the injection: (1) at the site of injection in sixty cases, (2) three interspaces above the site of injection in forty and (3) in the cisterna magna in twenty-two. The data indicate that the injected anesthetic is distributed rapidly cephalad. The peak concentration reached at a particular level during anesthesia decreases rapidly in the cephalad direction, so that in the cisterna magna the concentration of procaine was never above 0.21 mg. per cubic centimeter, and in fourteen of twenty-two samples it was less than 0.02 mg. These studies do not support the assumption that the Trendelenburg position causes concentrated solutions of procaine to flow down to the cisterna as do colored solutions in inanimate models.

Bulletin New York Academy of Medicine, New York

14: 583-652 (Oct.) 1938

- Studies on Cortical Representation of Somatic Sensibility. P. Bard, Baltimore.—p. 585.
Present Status of Gynecologic Endocrine Therapy. H. C. Taylor Jr., New York.—p. 608.
Pathologic Responses to Vitamin Deficiencies. G. Dalldorf, Valhalla, N. Y.—p. 635.
Our Vitamin B₁ Supply in Relation to Human Needs. R. R. Williams.—p. 641.

California and Western Medicine, San Francisco

49: 177-248 (Sept.) 1938

- Use of Dogs in Developing Treatment of War Gas Poisoning. P. J. Hanzlik, San Francisco.—p. 182.
Importance of Emergency Treatment of Compound Fractures. F. C. Bost, San Francisco.—p. 185.
Intratracheal Instillation of Liquid Petrolatum: Pulmonary Injury Therefrom. G. H. Houck, Los Angeles.—p. 187.
Cigarette Smoking: Its Effect on Volume and Acidity of Gastric Juice, with Particular Reference to Duodenal Ulcer. H. Rosenblum, San Francisco.—p. 191.
Physics: Its Application to Roentgen Therapy. R. E. Pugh Jr., Pasadena.—p. 194.
Human Rabies in California, with Discussion of Differential Microscopic Anatomic Diagnosis. J. C. Geiger and G. Y. Rusk, San Francisco.—p. 197.
Sulfanilamide: Its Use in Upper Genital Tract Infections in the Female. R. E. Gillett, San Francisco.—p. 206.
Id.: Its Use in Treatment of Gonorrhea of Lower Genital Tract of the Female. A. Manor, San Francisco.—p. 208.

Canadian Medical Association Journal, Montreal

39: 313-418 (Oct.) 1938

- Sir William Osler, Bt., M.D., F.R.S.: I. The Last Phase (1905-1919): II. His Influence on Medicine as a Whole. H. Rolleston, Haslemere, Surrey, England.—p. 313.
Goiter from the Standpoint of the General Practitioner. E. M. Eberts, Montreal.—p. 324.
Two Unrecorded Cases of Quintuplet Births, Canadian and Italian. N. Ford, Toronto, and G. Caruso, Palermo, Italy.—p. 333.
Syphilitic Ulcerations with Histologic Picture of Prickle Carcinoma Cured by Antiluetic Treatment. A. Marin and A. Bernier, Montreal.—p. 336.
Head Injuries: Treatise Considering Accidents of the Day. W. O. Stevenson, Hamilton, Ont.—p. 338.
Leber's Hereditary Optic Neuritis Through Six Generations: A Sterilization Problem. W. C. Whiteside, Edmonton, Alta.—p. 347.
*Experimental Study of Toxicity of Various Types of Quartz. D. A. Irwin and C. S. Gibson, Toronto.—p. 349.
Diagnosis of Heart Conditions in Early Childhood. A. P. Haist, Toronto.—p. 352.
Slipping Rib. H. C. Ballon and L. Spector, Montreal.—p. 355.
*Magnesium Trisilicate in Treatment of Peptic Ulcer. C. J. Tidmarsh and R. G. Baxter, Montreal.—p. 358.
Syphilophobia and Allied Anxiety States. F. E. Cornia, Montreal.—p. 361.
Anemia in Infancy. N. B. Coward, Halifax, N. S.—p. 366.
Three Cases of Diabetes Insipidus, One Associated with Toxic Goiter. H. McPhedran, Toronto.—p. 370.
The Young Myope. F. A. Aylesworth, Toronto.—p. 374.
Secondary Postappendicectomy Abscesses. W. A. Shandro, Vegreville, Alta.—p. 375.

Toxicity of Various Types of Quartz.—Irwin and Gibson collected fourteen samples of quartz from underground working faces of mines in the Sudbury, Kirkland Lake and Porcupine districts. These samples included all the types of quartz commonly encountered in mining operations in these districts. Each sample was ground to a fine powder and injected subcutaneously in 10 mg. amounts into rabbits. The tissue response produced at the sites of injection was studied at intervals up to two years and all the samples gave rise to a nodular fibrosis that was essentially the same in extent and degree.

Magnesium Trisilicate and Peptic Ulcer.—Tidmarsh and Baxter used a brand of magnesium trisilicate, which conformed with the standard requirements of Mutch for true artificial sepiolite, in the treatment of thirty-six patients. Each drachm of the preparation contained 35 grains (2.25 Gm.) of the trisilicate, which is the generally accepted dosage. The number of doses was regulated according to the gastric acidity and the clinical progress. There were nineteen cases of duodenal ulcer, three of duodenal ulcer with massive hemorrhage, four of gastric ulcer and ten cases of functional indigestion (hyperacidity and the like). Approximately 89 per cent of the patients were completely free from symptoms or improved as a result of treatment. Of the three patients with ulcers who failed to respond to treatment, one, after two months' observation and treatment, was operated on and a large duodenal ulcer penetrating deeply into the pancreas was found; the other two were improved so far as gastric symptoms were concerned but were obliged to stop the trisilicate because of diarrhea, which persisted in spite of reduced dosage. The patient with functional indigestion who failed to benefit had been taking Sippy powders for years for relief of indigestion due to cardiac disease, and the trisilicate was given as an adjunct to other therapy. Six patients with ulcers who were nervous and showed marked pylorospasm and spastic colon were given a special formula con-

taining, in addition to the 35 grains of magnesium trisilicate, $\frac{1}{500}$ grain (0.00013 Gm.) of atropine sulfate and one-eighth grain (0.008 Gm.) of phenobarbital to the drachm. These patients did not improve more rapidly than the others, but the mild antispasmodic sedative effects of the preparation brought about more restful nights, less apprehension and normal intestinal function.

Canadian Public Health Journal, Toronto

29: 425-476 (Sept.) 1938

- Contribution of Radiology to Cancer Problem. G. E. Richards, Toronto.—p. 425.
Tuberculosis Mortality and Morbidity in the Counties of Lincoln and Welland, Ontario. C. G. Shaver, St. Catharines, Ont.—p. 434.
Results of Immunization of Nurses Against Scarlet Fever. R. A. H. Mackeen and Rheta Wilson, St. John, N. B.—p. 439.
Blood Groups in Poliomyelitis. I. H. Erb, H. S. Doyle and F. C. Heal, Toronto.—p. 441.
Communicable Diseases; Past, Present and Future. J. K. McLeod, Sydney, N. S.—p. 443.
Control of Communicable Disease; Federal Responsibility. J. J. Cameron, Antigonish, N. S.—p. 446.
Demonstration of Types of Bacillus Typhosus by Means of Preparations of Type II Vi Phage: I. Principles and Technique. J. Craigie and C. H. Yen, Toronto.—p. 448.

Florida Medical Association Journal, Jacksonville

25: 105-156 (Sept.) 1938

- Preoperative and Postoperative Care of Intestinal Obstruction. H. A. Walker, Miami Beach.—p. 117.
Amebic Dysentery Carriers. M. J. Myres, Daytona Beach.—p. 122.
Hay Fever and Bronchial Asthma: Report of Cases. G. E. Henson, Jacksonville.—p. 125.
Florida Tuberculosis Control Program. J. A. Myers, Minneapolis.—p. 129.

Illinois Medical Journal, Chicago

74: 289-384 (Oct.) 1938

- Intussusception. P. Rosenblum, Chicago.—p. 309.
Some Pharmacologic Considerations of Intestinal Obstruction. C. A. Dragstedt, Chicago.—p. 313.
(Ileus) Intestinal Obstruction. J. A. Green, Rockford.—p. 315.
Some Physiologic Principles Involved in Acute Intestinal Obstruction. L. R. Dragstedt, Chicago.—p. 320.
Value of X-Ray Study in Acute Bowel Obstruction. J. T. Case, Chicago.—p. 326.
Surgical Treatment of Acute Intestinal Obstruction. H. E. Ross, Danville.—p. 331.
Strabismus. W. A. Fisher, Chicago.—p. 335.
Gynecologic Radium Therapy. H. Swanberg, Quincy.—p. 344.
X-Ray Therapy of Uterus and Adnexa. E. P. Halley, Decatur.—p. 350.
Studies on Mercurial Diuresis: Esidrone, a New Mercurial Diuretic. I. F. Volini and R. O. Levitt, Chicago.—p. 355.
Nonmyxedematous Hypothyroidism: Case Reported with Psychosis. G. A. Wiltrakis, Elgin, and A. V. Partipilo, Chicago.—p. 359.
*Pathology of Pneumonia: Review of 150 Cases of Lobar Pneumonia in 3,585 Autopsies. J. D. Kirshbaum, Chicago.—p. 362.
Progress in Maternal Welfare. H. H. Hill, Chicago.—p. 364.
Study of Treatment of Epilepsy. R. G. Novick, Jacksonville.—p. 366.
Neglected, Forgotten But Some Extremely Valuable Remedies Used by the Laity for Treatment and Supposed Cure of Pulmonary Tuberculosis During the Seventeenth, Eighteenth and Nineteenth Centuries. J. Ritter, Miami, Fla.—p. 369.

Pathology of Pneumonia.—Kirshbaum reviews the pathologic changes observed in 150 cases of lobar pneumonia found in 3,585 consecutive necropsies. The incidence of lobar pneumonia as the primary cause of death was 4.18 per cent. Lobar pneumonia was rare in children, while the peak was reached between 41 and 50 years and remained high up to 60 years. The upper part of the right lobe was most frequently involved, being affected in seventy-five cases. The lower part of the left lobe was second, being affected in seventy-two cases. In 70 per cent of the entire series two or more lobes showed consolidation. The stage of engorgement or hyperemia was not observed in any of the cases. This stage is usually present only during the first twenty-four hours of the disease. The changes usually observed were gray hepatization, which usually appeared at the end of the fifth day of illness, and red hepatization when more than one lobe was involved. The stage of resolution, which is the stage of healing, was practically absent except in those cases in which death occurred from some complication of the pneumonic process. Fibrinous pleuritis was found in eighty-two cases, jaundice in twenty-seven, lung abscess in seventeen, pericarditis in twelve, endocarditis in eight, empyema in five and cystitis in three. Clinically too much emphasis seems to be placed on the extent of the pneumonic process in the lungs, minimizing the bacteriologic studies. It is not as important

to know whether one or more lobes of the lung are involved as it is to know the causative organism present. The advances in the therapy of pneumonia depend to a great extent on definite bacteriologic studies. Bacteriologic studies were made in fifty of the 150 cases; sixteen showed pneumococci, streptococci of all types were present in fifteen, staphylococci of all kinds in seven, Friedländer's bacillus in five, Bacillus coli in four, B. influenzae in two, and Micrococcus tetragenus in one case. These bacteriologic studies show the high incidence of pneumonia due to organisms other than pneumococci, thus probably explaining the poor results obtained therapeutically in a large number of cases of pneumonia treated indiscriminately with pneumococcus serum.

Journal of Experimental Medicine, New York

68: 457-640 (Oct.) 1938

- Carcinoma in Leopard Frog: Its Probable Causation by a Virus. B. Lucké, Philadelphia.—p. 457.
Chemo-Immunologic Studies on Conjugated Carbohydrate-Proteins: XII. Immunologic Properties of Artificial Antigen Containing Cellobiuronic Acid. W. F. Goebel, New York.—p. 469.
Renal Insufficiency Following Trypsin Injection into Renal Arteries. M. Friedman and L. N. Katz, Chicago.—p. 485.
Studies on Sensitization of Animals with Simple Chemical Compounds: V. Sensitization to Diazomethane and Mustard Oil. K. Landsteiner and A. A. Di Somma, New York.—p. 505.
Pyogenic Filtrable Agent in Albino Rat. W. H. Woglom and J. Warren, New York.—p. 513.
Carcinogenic Effect of Papilloma Virus on Tanned Skin of Rabbits: II. Major Factors Determining the Phenomenon: Manifest Effects of Tarring. J. G. Kidd and P. Rous, New York.—p. 529.
Cellular Reactions to Polysaccharides from Tubercle Bacilli and from Pneumococci. F. R. Sabin, A. L. Joyner and K. C. Smithburn, New York.—p. 563.
Ultracentrifugation Studies on Elementary Bodies of Vaccine Virus: I. General Methods and Determination of Particle Size. E. G. Pickels and J. E. Smadel, New York.—p. 583.
Id.: II. Influence of Sucrose, Glycerol and Urea Solutions on Physical Nature of Vaccine Virus. J. E. Smadel, E. G. Pickels and T. Shedlovsky, New York.—p. 607.
Lymphatic Pathway from Nose and Pharynx: Absorption of Dyes. J. M. Yoffey and C. K. Drinker, Boston.—p. 629.

Journal of General Physiology, New York

22: 1-130 (Sept.) 1938. Partial Index

- Electrophoretic Mobility of Human Erythrocytes—Whole Cells, Ghosts and Fragments. W. H. Byler and H. M. Rozendaal, Schenectady, N. Y.—p. 1.
Intensity Discrimination in the Human Eye: II. Relation Between $\Delta I/I$ and Intensity for Different Parts of Spectrum. S. Hecht, J. C. Peskin and Marjorie Patt, New York.—p. 7.

Journal of Nervous and Mental Disease, New York

88: 397-568 (Oct.) 1938

- Psychologic Considerations of Insulin Treatment in Schizophrenia. L. L. Orenstein and P. Schilder, New York.—p. 397.
Morbid Hunger in Relation to Narcolepsy and Epilepsy. M. Levin, Mayview, Pa.—p. 414.
Relationship of Polydipsia and Polyuria in Diabetes Insipidus: Study of Experimental Diabetes Insipidus in Dogs With and Without Esophageal Fistulas. R. T. Bellows and W. P. VanWagenen, Rochester, N. Y.—p. 417.
Present Day Research Trends in the Field of Human Deficiency. E. J. Humphreys, Thiells, N. Y.—p. 474.
Sounds in Language. T. K. Davis, New York.—p. 491.
*Treatment of Epilepsy with Synergistic Combination of Phenobarbital and Belladonna. A. E. Loscalzo, New York.—p. 500.

Treatment of Epilepsy with Phenobarbital and Belladonna.—Loscalzo compared the effect of phenobarbital plus a mixture of potassium bromide and chloral hydrate, and phenobarbital plus levorotatory belladonna alkaloids in thirty-two cases of epilepsy (idiopathic) of unknown etiology. The patients were under observation for one year or more. During the first twenty-six weeks the patients were given from one-fourth to one-half grain (0.016 to 0.032 Gm.) of phenobarbital three times a day and more than half of the group received in addition daily doses of a mixture of $7\frac{1}{2}$ grains (0.5 Gm.) of potassium bromide and $7\frac{1}{2}$ grains of chloral hydrate. The dosage of phenobarbital was arbitrarily established, although attempts were made to adjust the quantity to the requirement of the individual patient. The number of seizures experienced was 804. An almost universal complaint was that the medication produced a state of lethargy and at times somnolence. During the second period of twenty-six weeks, as a test of the observations of Friedberg, the thirty-two patients were given tablets containing three-fourths

grain (0.05 Gm.) of phenobarbital and $\frac{1}{250}$ grain (0.00026 Gm.) of levorotatory belladonna alkaloids. The dosage was usually one-half tablet three times a day for those with less severe and less frequent seizures and four times a day for those of the moderately severe type and of more frequent occurrence, and one tablet three times a day for those whose condition necessitated the greatest degree of sedation. No other medication was employed. A total of 612 seizures occurred. There were no complaints of lethargy or somnolence except by the few patients who ingested the largest doses. About 40 per cent of these patients also stated that their convulsions now were much less severe. The patients were unaware of any change in medication aside from the fact that those who had previously taken both phenobarbital and the solution of bromide and chloral hydrate knew that the liquid had been discontinued. Consequently, any possible psychic effect was largely obviated. For the majority of patients the reduction in the number of seizures corresponded closely to the average result of slightly less than 24 per cent. Individual variations in response to the drug in a few cases, however, resulted in a decrease of from 50 to 60 per cent in the number of attacks, while in a limited number of less responsive patients a reduction of only from 5 to 10 per cent was noted. While there was a notable reduction in grand mal seizures, there was no alteration in the number of petit mal attacks. The results confirm the observations of Friedberg, Meggendorfer, Grinker, and Marchand and Viguier.

Kentucky Medical Journal, Bowling Green

36: 409-444 (Oct.) 1938

- *Control of Hemorrhage, with Special Reference to Moccasin Snake Venom. G. S. Buttorff, Louisville.—p. 411.
Hazards of Blood Transfusion. E. Allen Jr., Louisville.—p. 414.
Telangiectatic Edematous Myxofibroma of Nasopharynx. G. F. Doyle, Winchester.—p. 421.
Acute Abdominal Emergency. I. Abell Jr., Louisville.—p. 423.
Angina Pectoris. F. H. Russell, Wickliffe.—p. 426.
Pentothal Sodium for Intravenous Anesthesia. Gladys Smithwick, Lexington.—p. 427.
Multiple Pregnancy. G. F. Brockman, Shepherdsville.—p. 429.
The Doctor Before the Jury. J. H. Hendren, Pineville.—p. 430.
The Physiology of Hunger and Thirst. H. Lawson, Louisville.—p. 432.
The Next Great Battle for Soldiers of Medicine. H. A. Luce, Detroit.—p. 435.
Classification and Diagnosis of Nephritis. J. R. Gott Jr., Louisville.—p. 439.
Hematuria in Shoe Dye Poisoning. C. Baron, Covington.—p. 441.

Control of Hemorrhage with Snake Venom.—Buttorff cites a case of cholelithiasis with empyema and biliary obstruction, relieved by operation but complicated by a biliary fistula, severe jaundice and intractable hemorrhages of undetermined etiology. Repeated transfusions of blood gave only temporary relief. All other measures used failed to check the bleeding, and the patient was moribund until moccasin snake venom was used. Three days after the first (0.4 cc.) subcutaneous injection 0.6 cc. of the venom was injected and there was no further bleeding. Two further injections (0.8 and 1 cc.) were given at intervals of three days.

Nebraska State Medical Journal, Lincoln

23: 361-400 (Oct.) 1938

- Chronic Infectious Arthritis: Statistical Report of Findings and Treatment in Fifty Cases. M. J. Breuer, Lincoln.—p. 361.
Torsion of the Great Omentum: Report of Two Cases. C. Andrews, Lincoln.—p. 366.
Paranasal Sinus Disease in Children. S. Z. Faier, Omaha.—p. 370.
*Study of 836 Cases of Gallbladder Disease: Results of Medical and Surgical Treatment. J. D. Bisgard and R. G. Dornberger, Omaha.—p. 374.
Surgical and Hormone Treatment of Undescended Testicle. J. E. Courtney and J. W. Duncan, Omaha.—p. 381.
Treatment of Psychoses by Insulin and Metrazol. G. A. Young, Omaha.—p. 383.
Black Widow Spider Bite Treated with Calcium Intravenously: Case. C. T. Mason, Superior.—p. 389.

Gallbladder Disease.—Bisgard and Dornberger obtained data from the hospital records of 836 cases of extrahepatic biliary disease treated at the University Hospital from July 1925 to July 1936 and from the follow-up reports of the 434 patients who were traced. Of the 814 patients with benign lesions, 548 received operative treatment and 266 nonoperative dietary and medicinal therapy. In the surgical group there was a primary operative mortality of 5.4 per cent. Twenty-six patients were treated with cholecystotomy and follow-up

reports were obtained from eleven of them. Five were well, four improved and two were unimproved and became well only after subsequent cholecystectomy. Two patients have remained well for more than ten years. Follow-up reports were obtained from 287 patients treated by means of cholecystectomy with and without choledochotomy. The results in those with gallbladders containing stones were very good and were considerably better than those in the group with stoneless gallbladders. In the former group 78 per cent considered themselves well and 96 per cent were well or improved as compared to 60 and 87 per cent in the latter group. However, 23 and 12.8 per cent had residual symptoms of dyspepsia, leaving only 55 and 47.2 per cent entirely asymptomatic. The highest percentage of cures occurred in the cases of cholesterosis with stones and the lowest in those with histologically normal gallbladders. Of the patients with normal gallbladders, 54 per cent were well and 77 per cent were well or improved. A comparison of the results of cholecystectomy in the same group of 287 cases, classified in respect to the symptoms of dyspepsia and colic, showed that the percentage of both cures and improvements were much higher in the colic than in the nonecolic dyspeptic cases. This was true of all groups including cholesterosis and normal gallbladders. The difference, however, was much greater in the stoneless cases. Thus the degree and the likelihood of symptomatic relief by cholecystectomy is more dependent on the presence of stones or a history of colic than on the pathologic condition of the gallbladder. Reports from eighty-nine of the patients treated with nonoperative medical management show relief of symptoms in only 20 per cent and total asymptomatic relief in only 2 per cent. Nearly half of the entire group were unimproved. In both the surgical and the nonsurgical groups a large number of patients who considered themselves well continued to have some dyspepsia. Of the entire group of patients, 2.3 per cent were less than 20 years of age and 18 per cent were less than 30.

New York State Journal of Medicine, New York

35: 1257-1312 (Oct. 1) 1938

- Mandelic Acid Therapy. M. F. Campbell, New York.—p. 1257.
Carcinoma of the Right Half of the Colon: Diagnosis and Treatment. C. F. Dixon, Rochester, Minn.—p. 1262.
Treatment of Diabetes: Use of Protamine and Crystalline Insulin. H. J. John, Cleveland.—p. 1266.
Acute Peribronchiectatic Pneumonitis: Preliminary Report. R. A. Bendove and M. D. Deren, New York.—p. 1273.
The More Serious Vascular Affections: Etiology and Diagnosis. J. Gutman, Brooklyn.—p. 1278.
A Modified Nasal Catheter for Use in Oxygen Therapy. D. W. Richards Jr., New York.—p. 1283.
Boric Acid Dermatitis. A. Rothberg and G. A. Merrill, Brooklyn.—p. 1284.
Acute Appendicitis with Jejunal Intussusception and Abdominal Lymphadenitis: Occurring in a Child Immobilized in a Spica Plaster Cast: Report of Case. A. Lesser and L. R. Kaufman, New York.—p. 1285.
Homologous Popliteal Cysts Occurring in Identical Twins. P. D. Allen and P. Manjos, New York.—p. 1287.

Ohio State Medical Journal, Columbus

34: 1085-1196 (Oct.) 1938

- What Part Shall the Practicing Physician Take in the Campaign Against Syphilis? C. L. Cummer, Cleveland.—p. 1101.
Episiotomy: Technic of Repair. M. W. Diethelm, Toledo.—p. 1107.
Use and Abuses of Transfusion. W. D. Collier, Youngstown.—p. 1111.
Problems Associated with Reconstructive Procedures for Cleft Lip and Palate. J. O. Beavis, Dayton.—p. 1115.
Acute Poliomyelitis as Seen in a Recent Epidemic in Toledo, Ohio. H. G. Pamment, Toledo.—p. 1118.
Clinical Experiences with Insulin Therapy in Schizophrenia. R. F. Scherb and C. W. Stone, Cleveland.—p. 1120.
Nutritional Problems of the Preschool Child. R. A. Lyon, Cincinnati.—p. 1126.
Management of Obesity. E. P. McCullagh, Cleveland.—p. 1131.
Official Report of the Hospital Obstetrical Society of Ohio, for the Year 1937. B. Wylie, Lakewood.—p. 1136.
Activities of the Obstetrical Society of Dayton, Ohio. C. Sullivan, Dayton.—p. 1139.
Diabetes as an Obstetric Liability. T. P. Sharkey, Dayton.—p. 1141.

Rhode Island Medical Journal, Providence

21: 127-140 (Sept.) 1938

- Ulcer of the Stomach and Duodenum: Cancer of the Stomach. R. H. Miller, Boston.—p. 127.
Chemistry and Mode of Action of Sulfanilamide and Related Compounds. E. G. E. Anderson, Providence.—p. 131.
Convulsive Disorders in Childhood: Answers to Common Questions. C. Bradley, East Providence.—p. 135.

Southern Surgeon, Atlanta, Ga.

7: 385-488 (Oct.) 1938

- Some Experiences with the Flexible Gastroscope. J. L. Borland, Jacksonville, Fla.—p. 385.
Treatment of Malunited Fractures of the Ankle, with Special Reference to Fusion. W. C. Campbell, Memphis, Tenn.—p. 395.
Severe Hemorrhage of Peptic Ulcer Origin. J. R. Phillips, Houston, Texas.—p. 407.
Carcinoma of Upper Esophagus: Laryngectomy and Resection; Post-operative Mediastinitis with Drainage: Three Year Cure. M. Eguen and F. Neuffer, Atlanta, Ga.—p. 411.
Osteomyelitis. I. Cohn, New Orleans.—p. 415.
Review of 100 Cases of Acute Ruptured Peptic Ulcer. J. C. Read, Atlanta, Ga.—p. 436.
Surgical Dyspepsias. A. L. Lockwood, Toronto.—p. 443.

Southwestern Medicine, El Paso, Texas

22: 345-390 (Sept.) 1938

- Pulmonary Hypertension. T. J. Dry, Rochester, Minn.—p. 345.
Lesions of the Lips and Oral Cavity. L. M. Smith and R. P. Hughes, El Paso, Texas.—p. 349.
Congenital Umbilical Hernia: Report of Strangulated Case. W. J. Pangman, El Paso, Texas.—p. 351.
Intravenous Use of Fluids. H. C. Habein, Rochester, Minn.—p. 353.
Fractures of Spine with Injuries to the Cord. E. P. Palmer, Phoenix, Ariz.—p. 360.
Lead Absorption and Lead Poisoning. J. Rogde, El Paso, Texas.—p. 364.

Surgery, St. Louis

4: 483-648 (Oct.) 1938

- Experimental Observations on Surgical Treatment of Hypertension. H. Goldblatt, Cleveland.—p. 483.
Some Aspects of Blood Pressure Regulation and Experimental Arterial Hypertension. C. Heymans, Ghent, Belgium.—p. 487.
Essential Hypertension: Selection of Cases and Results Obtained by Subdiaphragmatic Extensive Sympathectomy. W. M. Craig, Rochester, Minn.—p. 502.
Blood Potassium During Experimental Shock. R. L. Zwemer and J. Scudder, New York.—p. 510.
Studies of Sodium, Potassium and Chlorides of Blood Serum in Experimental Traumatic Shock, Shock of Induced Hyperpyrexia, High Intestinal Obstruction and Duodenal Fistulas. J. D. Bisgard, A. R. McIntyre and W. Osheroff, Omaha.—p. 528.
*Survival of Clostridium Sporogenes, Bacillus Subtilis and Staphylococcus Albus on Surgical (Catgut) Ligatures. Katherine E. Hite and G. M. Dack, Chicago.—p. 548.
*Treatment of Undescended Testis, with Special Reference to Therapy with Hormones. C. E. Rea, Minneapolis.—p. 552.
Primary Retroperitoneal Tumors: Report of Three Cases and 107 Cases from the Literature. R. T. Frank, New York.—p. 562.
Hypertrophy of Ligamentum Flavum: Report of Two Atypical Cases. J. M. Meredith and E. P. Lichman, University, Va.—p. 587.
Subcutaneous Injuries of Intestine and Mesentery. H. P. Tolten, Los Angeles.—p. 597.

Survival of Bacteria on Ligatures.—Hite and Dack found that *Bacillus subtilis* when dried on surgical ligatures survives exposure to either toluene or alcohol for at least six months. *Clostridium sporogenes* survived in alcohol for six months but showed only slight resistance to the action of toluene. The experiments in general, however, indicate that any sporulating organism encountered in the routine sterility test might have been present on the ligature and should be considered as significant of possible contamination of the ligature, unless resampling indicates that they are sterile. *Staphylococcus albus* did not survive exposure to either toluene or alcohol for sufficiently long periods to be of significance to the contamination of ligatures, and on the basis of the experiments when encountered in the routine sterility test it indicates error in technic rather than contamination of the ligature.

Treatment of Undescended Testis.—Rea states that thirty patients with thirty-six undescended testes have been treated with antuitrin-S (Parke, Davis & Co.) at the University of Minnesota Hospitals. The ages of the patients varied from 4 to 24 years. The patients received 3,000 units of the preparation over a period of thirty days. Five patients with bilaterally retained testes responded to the treatment by degrees of descent of the testis into the scrotum. Descent was complete in three cases. It descended to only a high scrotal position in the other two cases. No untoward results have ever been observed over a period of two years following the use of antuitrin-S. There was suprapubic edema in three cases which disappeared after treatment and one patient complained of swelling in the left breast. In none of the cases was there a demonstrable increase

in the size of the penis. The testes of the successfully treated cases often enlarged. There seemed to be no change in the size of the testes in the unsuccessfully treated cases. The scrotum of one boy became red and slightly edematous after 2,000 units of antuitrin-S had been administered. In none of the cases was there premature appearance or increase in the amount of pubic, axillary or facial hair. Five patients noticed increased frequency of erections. Two patients, aged 21 and 23 years, were treated by follutein (Squibb) for undescended testes. The testes were bilaterally retained (inguinal) in one case and inguinally arrested on the right side in the other. One cc. of follutein (125 units) was injected daily for ten days into the subcutaneous tissue of the thigh. No improvement was noted following this therapy; the patients were observed for a period of one year. Three patients, aged 2, 7 and 11 years, were treated with prephysin (Chappell). The undescended testes were unilateral and inguinally retained. Prephysin contains the follicle-stimulating principle of the pituitary gland, including small amounts of the luteinizing factor. Five-tenths cc. of prephysin (12.5 units) was injected daily for four days into the subcutaneous tissue of the thighs of these three boys. No descent of the testis was observed over a period of nine months. Four patients have been treated with gonadotropic substance. The special strength solution, 500 units per cubic centimeter, has been used in doses of 0.5 cc. every other day until fifteen injections have been given. In three patients with unilateral inguinal testes, observed less than five months, no beneficial results have been seen. However, in the fourth patient, a boy 9 years old, with bilateral inguinal testes, complete descent of both testes occurred after the ninth injection. The extremes of puberty being 9 (Scammon) and 18 years (Crampton), treatment of the congenitally retained gland may be deferred until the patient is from 9 to 11 years old. It is the practice at the University of Minnesota Hospitals to try gonadotropic substance in all uncomplicated cases of undescended testes before surgical procedures are instituted. If, after six months of observation, no results have been observed with endocrine therapy, surgical treatment of the undescended testis is advised if the patient is 9 years of age or older. Endocrine imbalance alone does not fully explain the cause or give a rational basis for treatment in all cases of true testicular maldescent.

Texas State Journal of Medicine, Fort Worth

34: 323-390 (Sept.) 1938

- The Prevention of Heart Disease. J. Kopceky, San Antonio.—p. 331.
Modern Practical Methods in Treatment of Cardiac Decompensation. S. A. Shelburne, Dallas.—p. 335.
Nutritional versus Endocrine Factors in Bone Metabolism During Pregnancy. M. Bodansky, with assistance of Katherine Campbell and Virginia B. Duff, Galveston.—p. 339.
Result of Five Years' Experience with Desensitization for the Common Cold. L. A. Nelson, Dallas.—p. 343.
Fractures of the Skull: Study of 200 Cases. B. H. Bayer, Houston.—p. 346.
Certain Late Effects of Head Injuries. J. D. Gleckler, San Antonio.—p. 356.
Appendectomy Mortality: Brief Summary of 228,598 Cases. J. P. Barnes, Houston.—p. 360.
Relationship Between Allergy and Organic Pathology of Appendix. L. O. Dutton, El Paso.—p. 363.
Disease of Thyroid Gland and Its Pluriglandular Relationship. I. W. Jenkins, Waco.—p. 366.
Cancer Education. A. C. Scott, Temple.—p. 370.
Immunization Against Communicable Diseases: What, When and Why. J. G. Young, Dallas.—p. 372.

West Virginia Medical Journal, Charleston

34: 437-484 (Oct.) 1938

- Human Blood as a Therapeutic Agent. C. B. Chapman, Welch.—p. 437.
Organized Medicine versus Quackery. A. B. Collins, Blacksville.—p. 452.
Head Injuries. W. P. Sammons, Wheeling.—p. 462.

Wisconsin Medical Journal, Madison

37: 873-972 (Oct.) 1938

- Cholera Epidemics in Iowa County, Wisconsin. W. S. Middleton, Madison.—p. 894.
Complete Avulsion of the Scalp. W. F. Wilker, Iola.—p. 900.
Present Day Concepts in Diagnosis, Treatment and Prevention of Tuberculosis. J. A. Myers, Minneapolis.—p. 903.
Late Rupture of Extensor Pollicis Longus Tendon Following Colles' Fracture. W. P. Blount, Milwaukee.—p. 912.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

Brain, London

61: 237-338 (Sept.) 1938

- Pick's Disease: Specific Type of Dementia. I. C. Nichols and W. C. Weigner.—p. 237.
Thalamus of the Chimpanzee: III. Metathalamus, Normal Structure and Cortical Connections. A. E. Walker and J. F. Fulton.—p. 250.
Tonic Foot Response to Stimulation of the Sole: Its Physiologic Significance and Diagnostic Value. K. Goldstein.—p. 269.
Note on Nucleus Ruber Magnocellularis and Its Efferent Pathway in Man. K. Stern.—p. 284.
Local Sweat Response to Faradic Stimulation. R. W. Wilkins, H. W. Newman and J. Doupe.—p. 290.
Dissemination of Glioma of Spinal Cord in Leptomeninges. K. C. Eden.—p. 298.
Fibrillation and Fasciculation in Voluntary Muscle. D. Denny-Brown and J. B. Pennybacker.—p. 311.

British Medical Journal, London

2: 645-690 (Sept. 24) 1938

- Late Results of Partial Gastrectomy for Peptic Ulcer. J. Morley and F. H. Bentley.—p. 645.
*Prognosis of Anxiety States. A. Harris.—p. 649.
The Obstetric "Flying Squad." E. F. Murray.—p. 654.
Septal Deflection. W. S. Syme.—p. 656.
Calcium Mandelate and Sulfanilamide in Treatment of Urinary Infections. H. Droller.—p. 657.

Prognosis of Anxiety States.—Harris attempted to ascertain the present condition of 259 patients seen at the Maudsley Hospital during the years 1924, 1925 and 1926 in which the diagnoses were "anxiety neurosis," "anxiety state," "anxiety" "anxiety with depression" and "anxiety hysteria." Satisfactory follow-ups of 123 were obtained. Of these, thirty-eight were well, sixty were suffering from anxiety states, nine had developed psychoses and sixteen were dead. The main prognostic points elicited were that anxiety and its clinical manifestations may persist unchanged for ten years and over and that the percentage of cases in which it is converted to hypochondriasis is small. The prognosis is fairly good if the condition has lasted less than two years and, conversely, it is poor but not hopeless for ultimate and permanent recovery if the condition is of longer standing. The patient's chances of returning to work are always quite good, as only 20 per cent of those unable to work persisted in that state. If the patient's habits or mode of life remain substantially unchanged by the anxiety, the prognosis is good. The outlook for patients with markedly psychopathic personalities is poor. There was no evidence of increased susceptibility to organic disease.

Journal of Laryngology and Otology, London

53: 557-624 (Sept.) 1938

- Pathology of Nasopharyngeal Tumors. D. F. Cappell.—p. 558.
Some Observations on Relation Between Tests by the Voice, Gramophone Audiometer and Pure-Tone Audiometer. J. A. Keen.—p. 581.

Lancet, London

2: 705-760 (Sept. 24) 1938

- Radiography in Pneumonia: Diagnosis of Complications and Atypical Forms. F. G. Nicholas and C. D. Agassiz.—p. 705.
*The Rheumatic Lung. G. Hadfield.—p. 710.
Organic Gastric Syphilis: Review and Case Report. S. M. Laird.—p. 712.
Mitral Stenosis, with Chronic Passive Congestion Simulating Miliary Tuberculosis. A. F. W. Anglin.—p. 717.
*Action of Sulfanilamide on Leukocytes: Report on Fifty Ambulant Patients. C. J. C. Britton and J. Howkins.—p. 718.
Treatment of Urinary Infections in Puerperium. J. C. Cuthbert.—p. 720.
Technic for Spinal Anesthesia. O. S. Hillman.—p. 722.
Pneumoecranium: Two Cases. J. H. Pringle.—p. 724.

The Rheumatic Lung.—Hadfield makes two criticisms of the published histologic accounts of the rheumatic lung. 1. There is no clear description of the sequence of changes in the lung nor any attempt to correlate microscopic changes with the probable or approximate duration of the disease as determined from clinical data. 2. A considerable amount of histologic research has been concerned with discovering lesions which resemble the Aschoff node as it is seen in other tissues or in

finding changes in the pulmonary vessels of a specific kind such as those described by Pappenheimer and Glahn in 1924. The latter changes can be found in lungs in which rheumatic consolidation is absent and the Aschoff node as a clearcut lesion is difficult to identify in a loosely knit tissue like the lung, which in the intermediate stages of rheumatic consolidation is diffusely infiltrated by large mononuclear cells. The clinical features of rheumatic lung are as follows: The average age at death is 8.6 years. In 70 per cent of the patients death takes place during an acute exacerbation of a relapsing infection, the total average duration of which is one year. In 30 per cent the pulmonary consolidation complicates a first attack of virulent infection, the average duration of which is seven weeks. The final stage of acute dyspnea, which may be continuous or relapsing, varies from three to thirty days.

Action of Sulfanilamide on Leukocytes.—Britton and Howkins performed serial leukocyte counts of fifty ambulant patients receiving sulfanilamide in order to determine whether it produces any toxic leukocytic depression. After the usual routine clinical examination and a preliminary total blood count, the patient was given 0.5 Gm. of the drug three times a day for fourteen days, instructions being given to avoid saline purgatives and the foods containing sulfur. Serial total and differential leukocyte counts were made with ordinary standard pipets twice a week during the administration of the drug and for fourteen days subsequent to its cessation. All counts were carried out at the midfast period, between breakfast and lunch, to lessen the known daily fluctuations as much as possible. All precautions were taken to ensure the accuracy of the counts. The leukocyte count in thirty-two showed no marked variations—i. e., at no time was a leukopenia noted. In fourteen the count fell to between 5,000 and 4,000 per cubic millimeter of blood and in four to between 4,000 and 3,000. Of the total counts that fell below the threshold figure taken for leukopenia (5,000 per cubic millimeter) the lowest counts coincide with the end of the first week in two cases, the second week in three and the third week in nine. All four counts below 4,000 occurred in the third week. There was a tendency for the average total leukocyte count to fall steadily during the first week and to remain low for the next fortnight, rising to normal again by the end of the third week. The standard deviation of the counts observed on the different days of treatment was practically constant, being approximately $\pm 1,500$. In twenty-three patients the polymorphonuclear count at some time fell below 3,000; in twelve the figure fell below 2,500 and in five below 2,000. Invariably the lowest figure was found at the end of the second or beginning of the third week. The lymphocytes showed little or no change. In twenty-two cases the monocyte count rose above the upper normal level of 500 per cubic millimeter and in nine above 750. These changes were most common during the second and third weeks. An eosinophilia of more than 400 was observed in seven cases and in three it exceeded 500. Usually a rash accompanied this eosinophilia, but a moderately severe rash was at times unaccompanied by eosinophilia and vice versa. Thirty-five patients complained of toxic symptoms such as headache, dizziness, vertigo, depression, listlessness, somnolence and nausea, and tinglings in the hands and feet occurred. There was no definite relationship between such symptoms and any blood change. Two patients had marked dizziness accompanied by such a feeling of disorientation that they refused to walk in the streets alone. Such toxic symptoms were present most often in the first week and rarely in the second. Cyanosis occurred in nine cases but there was no relation to any blood change. Rashes were present in thirteen, in one of which cyanosis occurred. The rash was commonly urticarial in type and irritable. Both the rash and the cyanosis may disappear spontaneously even if the drug is continued.

Medical Journal of Australia, Sydney

2: 447-490 (Sept. 17) 1938

- Cellular Response to Injury. C. H. Kellaway.—p. 447.
Medicolegal Risks in Medical Practice. D. M. Morton.—p. 452.
Critical Survey of Renal Function Tests in Their Application to Determination of Renal Efficiency in Toxemias of Pregnancy. Vera I. Krieger.—p. 457.
Temperature as Factor to Be Considered in Clinical Urinometry. L. A. Windsor-McLean.—p. 467.

Presse Médicale, Paris

46:1417-1432 (Sept. 24) 1938

*Extracutaneous Localizations of Myxedema. G. Maranon.—p. 1417.
Malaria: Parasitic Reticulo-Endotheliosis. G. Sicault and A. Messerlin.—p. 1419.

Extracutaneous Localizations of Myxedema.—Maranon shows that myxedema, the typical lesion of thyroid insufficiency, not only involves the integument but attacks other parts of the organism as well, although with less frequency than the subcutaneous tissue. Myxedema is regarded as an infiltration of the tissues with mucin, a substance the formation of which is regulated by the thyroid hormones. Two factors are essential for correct diagnosis: 1. The supposed extracutaneous localization must coincide with other myxedematous manifestations. 2. The symptoms must disappear with the same promptness in response to thyroid therapy as do the cutaneous myxedematous lesions. The first type of extracutaneous localization of myxedema mentioned by the author is that which is localized in the nasal and pharyngeal mucosa. It produces dryness of the mucosa and difficulties in nasal respiration. Typical signs of this localization are the necessity of sleeping with the mouth open and sonorous snoring. If myxedematous infiltration exists in the buccal and lingual mucosa, it may produce dryness of the mouth. Another symptom is the hypertrophic and cracked appearance of the tongue and the loss of the sense of taste. The latter explains the lack of appetite in patients with hypothyroidism. Another symptom which may accompany the buccal and lingual localization of myxedema is a bad odor from the mouth. The author says that patients with hyperthyroidism often present deafness, buzzing in the ears and perhaps vertigo. Laryngeal localization, that is, infiltration of the mucosa of the vocal cords and of the larynx, probably explains to a great extent the faint tonality of the voice of patients with hypothyroidism. Many of the digestive disturbances presented by patients with myxedema, which have been attributed to secondary changes of the neurosympathetic system, in reality are due to direct visceral localization of the myxedema. He discusses the effects of myxedematous infiltration of the salivary glands, of the esophagus, of the gastric mucosa, of the anal mucosa and so on. He points out that in young persons the large myxedematous heart becomes entirely normal again following treatment with thyroid. He thinks that infiltration of the mucosa of the genitalia is quite frequent in women with hypothyroidism and thinks that this explains at least partly the frigidity of these patients. Finally he discusses infiltration of the nervous and of the locomotor system. Regarding the latter he says that in his material he found no definite proof of arthropathies of hypothyroid origin.

46:1433-1448 (Sept. 28) 1938

Vitamin B₁ in Treatment of Algeias. F. Coste and J. Metzger.—p. 1433.

*Treatment of Pulmonary Asthma by Ascorbic Acid (Vitamin C). D. Hagiesco, G. Bazavan, M. Criscota and M. Cioranescu.—p. 1435.
Return to Work and Social Future of Patients with Pulmonary Tuberculosis. A. Fabre.—p. 1438.

Treatment of Pulmonary Asthma with Vitamin C.—Hagiesco and his associates think that the unreliability of the results obtained heretofore in the treatment of pulmonary asthma justifies trials with new measures. Numerous investigations on vitamin C disclosed a number of pharmacodynamic actions which warrant its employment in disorders that have nothing in common with C-avitaminosis or C-hypovitaminosis. For instance, it has been proved that vitamin C is a powerful catalyzer, that it stimulates the activity of different ferments, that it contributes to the maintenance of the functional activity of the bone marrow and of the capillaries, that it possesses antitoxic and anti-infectious properties, that it influences the sympathetic nervous system, that it has a diuretic effect, that it influences the tonus of the heart and vessels and that it has a strong antianaphylactic action. Relative to the latter property the authors point out that in various pathologic disorders which are due to allergy it has been demonstrated that ascorbic acid diminishes the hyperergic manifestations as well as the modifications in the equilibrium of the blood proteins which are characteristic for these hyperergic conditions. They cite reports from the literature on the antianaphylactic action

of vitamin C and on its use in the treatment of asthma and then state that they used vitamin C in twenty cases of asthma, most of which were obstinate. In fifteen of these cases the results were good or favorable, while in the other five cases they were doubtful or negative. The authors give several case histories and then analyze the results. They take up separately the action on the individual attack, on a series of attacks and during a period of intermission. Regarding the action on the individual attack, they say that the injection of vitamin C has a suspensive action but that the return to a normal respiration is slow (from fifteen to thirty minutes) and even then may be incomplete. The intravenous injection is the only really effective mode of administration during the attack and the doses must be comparatively high. At the first injection from 200 to 300 mg. should be administered. If no improvement is observable after fifteen minutes, another dose of from 100 to 200 mg. may be given. About the effect of vitamin C on a series of attacks, the authors say that in the cases which react well to the vitamin C therapy the attacks cease entirely after from one to five injections and that the attacks always become less severe and prolonged. During the period of cessation the injections are continued intermittently. Patients with certain prodromal symptoms should have an injection every time that it seems necessary. It is advisable to give other patients at least five or six injections every month of 100 mg. each. The mode of administration is intravenous. The intramuscular injections are reserved for the periods of intermission and for the cases in which intravenous injection is impossible. The authors found that the oral administration of vitamin C has no antiasthmatic effect.

Sang, Paris

12:801-912 (No. 8) 1938

Agranulocytic Syndrome with Myeloblastoma and Reticulo-Endothelial Proliferation in Marrow, Viscera and Eyes. R. Waiz and G. Hoerner.—p. 801.

*Modifications of Blood Conserved for Several Weeks and Its Therapeutic Effect. H. Gnoinski.—p. 820.

Several Biologic Investigations on Catalase in Blood. H. Werner.—p. 832.

Modifications of Conserved Blood.—Gnoinski's investigations were aimed at determining under what conditions preserved blood is kept from undergoing hemolysis, what factors prolong the period of conservation, what changes take place in the blood during its conservation and finally how long blood can be conserved outside the organism and still be suitable for transfusion. His studies were made on the blood of forty dogs and on that of eighteen human subjects. The blood was examined before withdrawal, after the addition of sodium citrate, three hours later and finally at intervals of one, two, three and five days. It was found that the blood which is withdrawn in an aseptic manner and which at the time of withdrawal is mixed in the proportion of 1:5 with a 6 per cent solution of sodium citrate can be employed for more than eighty days if the following precautions are adhered to: 1. The blood must be kept in a hermetically closed container. 2. The blood must completely fill the container. 3. The container with the blood must not be subjected to shocks. 4. The blood must be kept in the refrigerator at a temperature of from 4 to 5 C. Studies on the erythrocytes revealed that some of the erythrocytes (about 15 per cent) are destroyed; others (about 40 per cent) undergo morphologic changes, and the remainder stay unchanged. The leukocytes were found to undergo considerable modifications in a rather short time. The blood which is conserved for more than sixty days is not toxic and it can be employed for transfusion without provoking disturbances. The author demonstrated this on six women. One of them was given a transfusion with blood that had been preserved for seventy-five days, another one with blood preserved for eighty-five days and the others with blood preserved for from sixty-four to sixty-six days. These transfusions demonstrated not only the harmlessness but also the great therapeutic value of conserved blood. It stimulates the hematopoietic system, which is proved by the increase in the number of erythrocytes. Encouraged by the results obtained so far, the authors plan to continue the clinical use of conserved blood.

Bullettino delle Scienze Mediche, Bologna

110: 141-208 (May-June) 1938. Partial Index

- Echinococcus of Liver and Spleen: Iconographic Study. G. Giordano and M. Boccioni-Giordano.—p. 150.
Importance of Functional Stimulation in Formation of Articular Cavity. C. Casuccio.—p. 168.
Surgery in Trigeminal Neuralgia. F. d'Ajutolo.—p. 182.
*Epidemiologic Importance of Carriers of Diphtheria Bacilli. A. Rosa and A. Chieco.—p. 190.

Epidemiologic Importance of Carriers of Diphtheria Bacilli.—Rosa and Chieco made investigations on identification of diphtheria bacilli in a group of children who were living in Bologna in a government home for children of tuberculous families. The Schick test performed on 120 children gave positive results in forty-eight cases and negative results in seventy-two cases. One week later one of the children became ill with diphtheria and was transferred to the hospital. After this event seroprophylaxis was carried out in all children. Search for diphtheria bacilli showed the presence of forty-nine carriers in the group. Both the mild and intermediate types were identified. In eight cases diphtheria bacilli of both the mild and intermediate types coexisted. Forty-eight strains of the bacilli which were identified in the carriers killed guinea pigs. Forty-six strains killed the animals within three days and two strains killed them within six days. The author emphasizes the epidemiologic importance of carriers.

Clinica Ostetrica, Rome

40: 437-492 (Sept.) 1938

- *Pulmonary Tuberculosis and Menstrual Disturbances. L. Praloran.—p. 437.
Spontaneous Delivery of Fetus in Shoulder Presentation: Case. G. Betto.—p. 444.
Pathogenic Mechanism of Tuberculous Salpingitis by Peritoneo-Adnexal Diffusion. A. Fortunato.—p. 451.
Utility of Intraparenchymal Uteral Injections of Posthypophyseal Extract in Comparison with Uterovaginal Packing. E. Giudici.—p. 468.

Pulmonary Tuberculosis and Menstruation.—Praloran studied the relations between pulmonary tuberculosis and menstrual disturbances in a group of 620 women. Those who had menstrual disorders before the development of pulmonary tuberculosis, as well as those who were suffering from gynecologic diseases, were excluded from the group. The author concludes that women with pulmonary tuberculosis and menstrual disturbances may have benign tuberculosis of the genitalia, which is the cause of the menstrual disturbances. Frequently, however, the irregularities of menstruation, especially amenorrhea, oligomenorrhea, hypermenorrhea and metrorrhagia, depend on the intensity of tuberculous toxemia and subside as the lesions of pulmonary tuberculosis improve with the administration of a proper treatment. In menstrual disturbances, either grave or of long duration, it is advisable to resort to treatment for pulmonary tuberculosis. Menstrual (especially premenstrual) increase of the temperature is frequent in 20 per cent of the cases in pulmonary tuberculosis and the appearance of menstrual hemoptysis is frequent in 3 per cent of the cases. The general (sensory, gastric, cardiac and circulatory) phenomena follow a normal behavior in the course of pulmonary tuberculosis.

Minerva Medica, Turin

2: 245-268 (Sept. 15) 1938

- Behavior of Polypeptides, Sugar and Urea in Blood in Diabetes After Administration of Peptone Before and After Insulin Treatment. R. Locascio.—p. 245.
Early Roentgen Diagnosis of Gastric Cancer. F. Gagna.—p. 247.
*Intravenous Pyelography and Chromoscopy for Renal Functions. S. Biancardi.—p. 254.

Tests for Renal Function.—Biancardi states that chromoscopy by indigo carmine is a more sensitive test than descending pyelography for the measurement of renal function. The author carried on a comparative study of the elimination, in the same patient, of indigo carmine and the opaque substance which was intravenously administered for descending pyelography. The observations were made in a group of 150 cases which included pyelonephritis, renal ptosis, hydronephrosis from either renal ptosis or ureteral or pelvic calculi, calculous and other forms of pyonephrosis and hydropyonephrosis, renal tuberculosis, renal tumors, hematuria, renal ectopia, contusion, cystitis and some other renal diseases. He found that grave

alterations of the renal parenchyma are shown by disturbances of the same intensity in the elimination of the indigo carmine and of the opaque substance. When the parenchyma is slightly involved the elimination of the pyelographic substance is normal, whereas indigo carmine is either insufficiently eliminated or not eliminated at all.

Archiv für klinische Chirurgie, Berlin

192: 545-686 (Sept. 6) 1938. Partial Index

- Delayed Emptying of Ileum and Stasis in Chronic Appendicitis. S. Teneff.—p. 545.
*Significance of Relationship of Openings of Biliary and Pancreatic Ducts to Each Other in Causation of Gallstones. H. Mehnen.—p. 559.
Internal Biliary Fistulas Developing on Basis of Ulcer. F. Köberle.—p. 572.
Effect of Denervation of Hepatic Hilus and Renal Hilus on Abscess Formation in Liver and Kidney. U. Kawabata.—p. 595.
*Gastric Acidity After Operations for Gastric Duodenal Ulcer with Particular Attention to Relation Between Operative Result and Postoperative Gastric Secretion. M. Tomoda and J. Aramaki.—p. 604.
Echinococcus of Ovary and Omentum in Woman Operated on Six Years Previously for Gastric Cancer. Mátyás Mátyás.—p. 631.

Openings of Biliary and Pancreatic Duct and Causation of Gallstones.—Mehnen describes four different types of the opening of the common bile duct and the pancreatic duct into the intestine. He had investigated 449 cases and found a separate opening into an individual papilla in nineteen, a separate opening into a common papilla in 151 cases and a common opening with formation of a diverticulum in 248 cases, while in twenty-seven cases the pancreatic duct and the choledochus entered the duodenum about 8 mm. away from the papilla of Vater without formation of a diverticulum. Thus the anatomic relationships found made it possible in 61.25 per cent of the cases for regurgitation of pancreatic juice into the gallbladder in the cases of obstruction in the opening of the ducts into the intestine. The author had established that among the 275 cases presenting the possibility of regurgitation of pancreatic secretion there were 35.3 per cent instances of gallstones, while in 174 cases with separate openings the stones were found in only 14.4 per cent. The incidence of cholesterol-pigment-calcium stones in joint opening of the ducts as opposed to that of cases in which there was no possibility for back flow was as 4:1 and the incidence for pure cholesterol stones as 7:1, while for pure pigment stones it was as 1:5. The author investigated 200 cases with regard to the gallbladder content. The characteristic sediment in cases of joint opening of the large ducts consisted of cholesterol crystals, while that for the separate openings were bilirubin concrements. The author interpreted these observations by assuming that the regurgitation of the pancreatic juice into the gallbladder leads to diminution of biliary acids and therefore to precipitation of cholesterol, which in turn favors the formation of cholesterol-pigment-calcium stones and particularly the formation of pure cholesterol stones. The fact that of the twenty-nine cases of strawberry gallbladder twenty-five presented the possibility of regurgitation of pancreatic juice supports the concept of the disturbance of the solubility of cholesterol through the regurgitation of pancreatic secretion.

Gastric Acidity After Operations.—Tomoda and Aramaki report a study of gastric secretion before and after operation in 135 cases of gastric-duodenal disease carried out for periods of from several weeks to thirteen years after operation. The figures obtained for the acidity in thirty-two cases of gastro-enterostomy were not uniform. This operation has failed to lower the acid values. In the majority of the cases the authors found either normal or excessive values. The anacidity occurred very seldom after a gastro-enterostomy. They found in twenty-nine cases of resection for exclusion that the free hydrochloric acid was absent or markedly lowered independently of whether one practiced mucoclasia of the mucosa of the antrum or not. The free hydrochloric acid was either absent or markedly lowered in seventy cases following stomach resection. The authors found that the success or failure of an operative procedure on the stomach did not have a clear relation either to the lowering or to the increasing of the acid values. The consideration of the acid values alone in a stomach that has been operated on has no value in determination of the success or failure of a given operation. Equally unreliable is the assumption that the complaint of heartburn or gastric pain is characteristic of hyperacidity. A number of surgeons, and of late

particularly Max Friedemann, insist, however, that a diminution or increase of free acid after operation is essential to good results. This, however, is a purely empirical and not a scientifically proved assertion. Conclusions as to the secretion of the stomach stump based alone on the consideration of the acid values in aspirated stomach contents are unreliable. The observations of the Portises, of Enderlen and Zukschwerdt and of Shapiro support this view. From their studies it is evident that the first phase of secretion presents no qualitative alteration and that the second phase is compensated by the intestine. Shapiro's observations that even the subtotal gastric resection does not result in lasting lowering of the hydrochloric acid secretion and cannot therefore prevent the development of new ulcers deserve particular attention. It has been established recently that extensive gastric resection gives the best results. However, there is no scientific explanation for the failure or success of this operation. The authors feel that their investigation contradicts the widely accepted but definitely empirical explanation for the success or failure of the wide resection.

Deutsche medizinische Wochenschrift, Leipzig

64: 1277-1312 (Sept. 2) 1938. Partial Index

- Significance of Anamnesis for Diagnosis of Cerebral Tumors. P. Vogel.—p. 1277.
Nursing at the Breast and Prophylaxis and Therapy of Mastitis. R. K. Kepp.—p. 1281.
Treatment of Hemophilia with Female Sex Hormone. A. Kocsis and A. Hasskő.—p. 1284.

Treatment of Hemophilia with Female Sex Hormone.—Kocsis and Hasskő point out that since women do not show the symptoms of hemophilia although they transmit it to their offspring, it has been concluded that the sex apparatus and the endocrine system of women prevent the manifestation of the disease. Consequently attempts were made to counteract hemophilia by means of female sex hormones. They describe case histories and then take up the dosage, pointing out that during a hemophilic hemorrhage from 500 to 1,000 mouse units of female sex hormones must be administered daily. They maintain that the best results are obtained by the intravenous injection of a preparation that contains all the hormones of the ovaries, but that the subcutaneous injection into the extensor surface of the thigh is the more simple method. During severe hemorrhages, 500 mouse units may be administered by intramuscular injection twice daily and the action of this treatment can be supported by corpus luteum tablets. The capacity of the ovarian hormone to arrest hemorrhage and promote coagulation was proved also when it was administered locally, for instance in tooth extractions. In vitro tests corroborated the coagulating effect of ovarian hormone extract on hemophilic blood.

Monatsschrift für Kinderheilkunde, Berlin

75: 1-176 (Sept. 9) 1938. Partial Index

- Convulsions During Childhood: Pathologic Anatomic Studies. W. Scholz.—p. 5.
Modification of Convulsions During Early Childhood by Means of Roentgen Irradiation. E. Wittermann.—p. 44.
After Examinations on Children With and Without Intracranial Hemorrhages Sustained During Birth. S. Liebe.—p. 47.
Recurring Intestinal Diseases During Childhood. K. Hassmann.—p. 67.
Clinico-Experimental Investigations on Respiration in Fresh Air Treatment of Pneumonia. J. Jochims.—p. 73.
Demonstration of Viruses in Rubella, Epidemic Parotitis and Aphthous Stomatitis. H. Steinmauer.—p. 98.
Experiences with Prophylaxis of Measles by Means of Placental Extract. H. G. Huber and M. Kurz.—p. 106.
Prophylaxis of Rickets in Premature Infants by Means of Single Large Dose of Vitamin D. Windorfer.—p. 124.

Viruses in Rubella, Mumps and Aphthous Stomatitis.—Steinmauer reports that he demonstrated viruses in three children's diseases in which this had not been done before. His work was greatly facilitated by fluorescence microscopy, the latest improvement in this sphere. In twenty children with rubella he examined specimens of the nasal and pharyngeal secretions and of the blood beginning with the day of the appearance of the eruption. Moreover, cantharis blisters were produced in the majority of these children. Specimens were examined daily from the children who had been exposed, beginning from the first day of incubation. The examinations were continued even after the disappearance of the exanthem. On the day of the exanthem the author detected large quantities of

extremely small but well differentiated forms of a virus in the nasal and pharyngeal specimens in all cases. The virus was demonstrated also in the blood. Here the virus bodies were partly free and partly phagocytized by leukocytes. The virus was obtained in pure form from the lymph of the cantharis blisters. The author says that he examined all specimens under the fluorescence microscope as well as after staining with victoria blue and some also after staining according to Morsow's method. Identical results were obtained, except that the stained specimens were sometimes diluted and consequently less clear than the primulin preparations. The author considers it as especially noteworthy that the nasopharyngeal specimens were almost free from the usual bacterial flora at the time when the virus was present in large quantities, whereas the ordinary bacterial flora was present when, during the earlier or later stages, the virus was present in smaller quantities. The serial examinations revealed that the quantity of virus increased greatly one or two days before the appearance of the exanthem and reached the peak on the day of the eruption of the exanthem; it completely disappeared two or three days afterward. The author regards these always recurring fluctuations as a proof for the etiologic significance of the demonstrated virus. He mentions also that it proved possible to cultivate the virus on the chorio-allantois of the incubated hen's egg, which proves that the detected granules are of the nature of a virus and not merely a lifeless substance. In studies on the saliva of eighteen children with mumps, he demonstrated a virus which is considerably larger than that of German measles. This virus likewise could be cultured in egg medium. Finally, the author demonstrated virus bodies in specimens obtained from the aphthae of nine patients with aphthous stomatitis.

Nederlandsch Tijdschrift v. Geneeskunde, Amsterdam

82: 4151-4294 (Aug. 27) 1938. Partial Index

- Foundations of Treatment of Exophthalmic Goiter. H. Feriz.—p. 4157.
Occurrence of Abnormally Large Quantities of Testis Hormone in Urine of Patients with Adrenal Tumor. E. Dingemans and E. Laqueur.—p. 4166.
Typhoid in Volendam. H. Peeters and A. Charlotte Ruys.—p. 4171.
Zinc as Cause of Food Poisoning. C. G. J. Dornickx.—p. 4185.

Testis Hormone in Patients with Adrenal Tumor.—Dingemans and Laqueur say that the clinical picture of virilism in women suggests that an increased production of testis hormone (comb growth promoting substance) might be a causal factor in this condition. In several cases of hirsutism without adrenal tumor they were able to detect a moderate increase in the testis hormone content of the urine. Whereas the normal testis hormone content of the urine varies between 40 and 50 international units per liter, in women with hirsutism it was found to be between 75 and 150 international units. In three patients with adrenal tumor the testis hormone content of the urine varied between 600 and 2,200 international units and the diagnosis of tumor of the adrenals was corroborated by pathologic-anatomic observations. The authors cite three other cases of hirsutism in which an adrenal tumor was suspected. The results of the determination of testis hormone in the urine of these patients did not justify the diagnosis of tumor of the adrenals. The authors admit that their material is as yet too small to warrant generalizing conclusions. Nevertheless, they regard the large quantities of comb growth promoting substance excreted by the three patients with hypernephroma as worthy of attention. In the other patients with hirsutism of different, mostly unknown, origin the testis hormone content was only moderately increased. It is suggested that a simultaneous increase in the estrogenic substances may prove to be of diagnostic value.

Zinc as Cause of Food Poisoning.—Dornickx reports that more or less severe symptoms of poisoning developed in twenty-five of forty-two men who had eaten of the same food at a table for junior officers. Bacteriologic tests proved negative, but chemical tests revealed 83 mg. of zinc in 100 Gm. of cooked apples and 17 mg. of zinc in 100 Gm. of vomit. Inquiries disclosed that the dried cooked apples which had been served at the meal had been cooked in a kettle of galvanized iron, from which they absorbed considerable quantities of zinc. The author reviews the literature on zinc poisoning and reaches the conclusion that cooking utensils should not be made of galvanized iron.

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Clotting Power of Blood in Relation to Vitamin K.—Dam and Glavind direct attention to the fact that a method for the determination of the clotting power of avian blood on addition of tissue extract from the same or related species was described by Albert Fischer in 1930. This method is utilized in the assay of vitamin K. The authors adapted this method for human and mammalian blood in which the thrombocytes normally play an important part in the clotting process. To prevent clotting before the determination can be made, heparin is added to the blood. The coagulation deficiency is expressed by the quotient $R = \frac{K}{K_n}$, K representing the concentration of

the tissue extract which under fixed conditions produces clotting of the plasma in three minutes, while K_n represents the corresponding concentration for a normal plasma. The authors show further that it is possible to develop in rabbits a mild degree of K avitaminosis by means of a K-free diet. Then they describe how they used the aforementioned method for the determination of the clotting power of the blood of patients with various diseases. In essential thrombopenia and hemophilia the blood plasma was found to have normal R values when tested by this method, which does not register cellular anomalies. In obstructive jaundice a reduction of the clotting power could be demonstrated. In some of these cases the R values were considerably increased. The coagulation deficiency in obstructive jaundice was investigated with respect to its relation to the dietary K avitaminosis in chicks. The R values of mixtures of plasma in cases of obstructive jaundice and of normal plasma had great resemblance to those of mixtures of plasma from chickens with K avitaminosis and of plasma from normal chickens as well as of mixtures of plasma that was free from prothrombin and of normal chicken plasma. Obstructive jaundice was produced in normally fed chickens by ligation of the choledochus. Rapid increase of the R values occurred about twenty-four days after the occlusion of the choledochus. It was possible to restore the clotting power to normal values (reduce the R value to about 1) by one single intracardial injection of a K vitamin concentrate. In five cases of obstructive jaundice in patients with rather high R values the clotting power was rendered normal by from three to five intramuscular injections of emulsions of vitamin K. Discussing the etiology of the clotting deficiency in obstructive jaundice, the authors point out that vitamin K and other fat soluble substances are poorly absorbed when bile is absent.

Sympathico-Endocrine Insufficiency.—Under the term of sympathico-endocrine insufficiency Engelkes describes a syndrome of which he could find no description in the literature. He reports the clinical histories of two cases. The first one concerned a man, aged 41, who became acutely ill in October 1932. On waking up one morning he found his face, hands and feet swollen. This was accompanied by numbness of the extremities. Soon after this an intense cyanosis developed all over the body, which was maximal on the peripheral parts: hands, feet, ears and nose. This cyanosis was not accompanied by dyspnea. The possibility of a poisoning was considered. On spectroscopic examination of the blood, however, no changes of the hemoglobin were found. Extensive cardiologic examination revealed no changes of the heart. A marked enlargement of the liver and spleen was found, but there was no ascites. During the subsequent months edema developed and an increasing disturbance of the gait, owing to a polyneuritis. The patient became progressively emaciated. During the months from January to June a gradual decline occurred in his condition; his legs became paretic, his arms in a less degree. Sensitivity

was impaired below the knees, the disturbance increasing toward the periphery. The cyanosis of the skin gradually gave way to pigmentation. Two months later he complained of severe pain in the lower extremities, excessive tiredness, and at times duodenal epigastric pain. His appetite was fair. Often he was drowsy and could sleep for days at a stretch. Emaciation was excessive. The skin showed a pigmentation completely corresponding in color and distribution with that found in Addison's disease. The legs were edematous and of a livid color and were kept in an equinus position. The four smaller toes of the right foot on their dorsal aspect showed gangrenous ulcers. On treatment it soon became clear that digitalis and diuretics did not influence the edema. A diet rich in vitamin C and the vitamins of the B group was given. When no more improvement was obtained with these, adrenal cortex extract was added. Soon, however, bronchopneumonia developed to which the patient succumbed after an illness of twenty-three months. The clinical picture presented by the second patient, apart from minor details (absence of pigmentation and increased basal metabolism), completely corresponded to that of the first case; that is, the disorder began with a rather acute stage, with acrocyanosis and congestion of the abdominal organs. This was followed by a more chronic stage in which these signs gradually decreased and a severe polyneuritis developed, with edema, trophic ulcers and endocrine disturbances, especially of an adrenal nature. In the second case a necropsy was performed but nothing was found which would explain the severe disorder. Slight changes were detected only in the subthalamus. The author thinks that the symptoms can be explained as a disturbance in the sympathetic innervation, most probably resulting from a primary lesion of the sympathetic basal ganglions in the midbrain. He suggests that the term sympathico-endocrine insufficiency best characterizes the disorder.

Rheumatic Fever and Nephritis.—Salvesen draws attention to rheumatic nephritis, a form of nephritis which develops during or shortly after an attack of rheumatic fever or, in rare cases, immediately preceding it. He reviews the clinical histories of six cases classified as rheumatic nephritis. Only the first of these cases, which is given in detail, differs somewhat in its clinical aspects from cases of acute glomerular nephritis. It started as an ordinary post-tonsillitic rheumatic fever, but after a few days azotemic uremia with almost complete anuria developed and at the same time all the signs of rheumatic fever, including the increased temperature and the articular symptoms, disappeared but returned again with renewed force when the renal function became normal. In the second case the subchronic glomerular nephritis, which was diagnosed after the articular symptoms had disappeared, developed into uremia, during which new articular symptoms appeared. In the third case typical rheumatic fever was followed by afebrile hemichorea, and the symptoms of acute nephritis developed immediately after the choreatic symptoms had ceased. In the other cases the symptoms were those of ordinary acute and chronic glomerular nephritis with hypertension and hematuria. None of the patients had the lumbar pain that is said to be characteristic of rheumatic nephritis. The lumbar pain was lacking also in the ten cases of rheumatic nephritis which were found among the 212 cases of rheumatic fever which were treated at the clinic. The author says that rheumatic nephritis seems to be more frequent than was supposed formerly, because at his clinic ten cases were detected among 212 cases (4.7 per cent) of rheumatic fever and six cases among 287 patients (2 per cent) who entered the clinic with the diagnosis of nephritis. He points out further that salicylates have been regarded as a causal factor of renal symptoms. However, Rosenthal, who investigated this question in 420 cases of rheumatic fever, emphatically denies a deleterious action of salicylates on the kidneys. Edström calls attention to a considerable parallelism between diffuse glomerular nephritis and rheumatic fever as regards not only the pathogenesis and epidemiology but also the geographic distribution, the seasonal variations and to a certain degree also the age incidence. It might therefore be more than a coincidence that rheumatic fever was found in the history of twenty-nine of 287 cases of acute and chronic nephritis, of which six are described in this paper as rheumatic nephritis, while seventeen were chronic with unknown etiology and onset, and rheumatic valvular disease and hypertensive nephritis occurred simultaneously in seven of these.

